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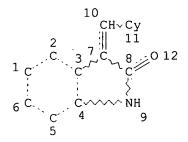
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NODE ATTRIBUTES: DEFAULT MLEVEL IS ATOM DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES: RSPEC I NUMBER OF NODES IS 12

STEREO ATTRIBUTES: NONE

L5
4211 SEA FILE=REGISTRY SSS FUL L3
L7
208 SEA FILE=HCAPLUS ABB=ON PLU=ON L5
L11
361 SEA FILE=REGISTRY ABB=ON PLU=ON ANGIOGEN? OR FH1 OR FLK?
L12
17556 SEA FILE=HCAPLUS ABB=ON PLU=ON L11 OR ?ANGIOGEN? OR FH1 OR FLK? OR FH(W)1
L14
16 SEA FILE=HCAPLUS ABB=ON PLU=ON L7(L)L12

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L14 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 2001:416904 HCAPLUS

DOCUMENT NUMBER:

135:19497

TITLE:

INVENTOR(S):

SOURCE:

Preparation of curcumin analogues for treating cancer Snyder, James P.; Davis, Matthew C.; Adams, Brian; Shoji, Mamoru; Liotta, Dennis C.; Ferstl, Eva M.;

Sunay, Ustun B.

PATENT ASSIGNEE(S):

Emory University, USA PCT Int. Appl., 69 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KI				ND	DATE			APPLICATION NO.					DATE					
WO	2001040188			A1		20010607			WO 2000-US32870					20001204				
	W:	ΑE,	AG,	AL,	AM,	ΑT,	ΑT,	ΑU,	ΑZ,	ΒA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	
		CN,	CR,	CU,	CZ,	CZ,	DE,	DE,	DK,	DK,	DM,	DZ,	EE,	EE,	ES,	FI,	FI,	
		GB,	GD,	GE,	GH,	GM,	HR,	ΉU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	
		ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	LV,	ΜA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	
		NO,	NZ,	PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SK,	SL,	ТJ,	TM,	TR,	
•		TT,	ΤZ,	UA,	UG,	US,	UZ,	VN,	YU,	ZA,	ZW,	AM,	AZ,	BY,	KG,	ΚZ,	MD,	
		RU,	ТJ,	TM														
	RW:	GH,	GM,	ΚE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	ΤZ,	UG,	ZW,	AT,	BE,	CH,	CY,	
		DE,	DK,	ES,	FΙ,	FR,	GB,	GR,	ΙE,	ΙT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	
		ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	G₩,	ML,	MR,	ΝE,	SN,	TD,	TG			
PRIORITY APPLN. INFO.:					US 1999-168913 P								P	19991203				
OTHER SOURCE(S):					MARPAT 135:19497													
GI																		

Curcumin analogs of formula I [Y = OH, halo, CF3; Z = H, (substituted) OH,AΒ halo, CF3; X1, X2 = C, N; A = CHCOCH, NHCONH, CHCH(OH)CH, R1, R2, etc.]

are prepd. which exhibit antitumor and anti-angiogenic properties. Thus, II was prepd. from cyclohexanone and 2-hydroxybenzaldehyde. The growth inhibitory concn. of II in the NCI anti-tumor screen was lower than CISPLATIN for several cell types.

IT 3367-88-2P 342808-37-1P 342808-38-2P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of curcumin analogs as antitumor and anti-angiogenic agents)

REFERENCE COUNT:

2

REFERENCE(S):

- (1) El-Subbagh; J MED CHEM 2000, V43(15), P2915 HCAPLUS
- (2) Teuscher, E; PHARMAZIE 1987, V42(2), P109 HCAPLUS

L14 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

2001:169669 HCAPLUS

DOCUMENT NUMBER:

134:348057

TITLE:

The antiangiogenic protein kinase inhibitors SU5416 and SU6668 inhibit the SCF receptor (c-kit) in a human

myeloid leukemia cell line and in acute myeloid

leukemia blasts

AUTHOR(S):

Smolich, Beverly D.; Yuen, Helene A.; West, Kristina A.; Giles, Francis J.; Albitar, Maher; Cherrington,

Julie M.

CORPORATE SOURCE:

Sugen, South San Francisco, CA, 94080, USA

SOURCE:

Blood (2001), 97(5), 1413-1421 CODEN: BLOOAW; ISSN: 0006-4971

PUBLISHER:
DOCUMENT TYPE:

American Society of Hematology

LANGUAGE:

Journal English

SU5416 and SU6668 are potent antiangiogenic small-mol. inhibitors of AB receptor tyrosine kinases, including those of the vascular endothelial growth factor and platelet-derived growth factor receptor families. The stem cell factor (SCF) receptor, c-kit, is structurally related to these receptors and, although not expressed on mature peripheral blood cells, is expressed in leukemic blasts derived from 60% to 80% of acute myeloid leukemia (AML) patients. The c-kit kinase inhibitory activity of SU5416 and SU6668 was evaluated in MO7E cells, a human myeloid leukemia cell Tyrosine autophosphorylation of the receptor, induced by SCF, was inhibited in these cells by SU5416 and SU6668 in a dose-dependent manner (inhibitory concn. of 50% [IC50] 0.1-1 .mu.M). Inhibition of extracellular signal-regulated kinase 1/2 (ERK1/2) phosphorylation, a signaling event downstream of c-kit activation, was also inhibited in a dose-dependent manner. Both compds. also inhibited SCF-induced proliferation of MO7E cells (IC50 0.1 .mu.M for SU5416; 0.29 .mu.M for SU6668). Furthermore, both SU5416 and SU6668 induced apoptosis in a doseand time-dependent manner as measured by the increase in activated caspase-3 and the enhanced cleavage of its substrate poly(ADP-ribose) polymerase. These findings with MO7E cells were extended to leukemic blasts from c-kit+ patients. In patient blasts, both SU5416 and SU6668 inhibited SCF-induced phosphorylation of c-kit and ERK1/2 and induced apoptosis. These studies indicate that SU5416 and SU6668 inhibit biol. functions of c-kit in addn. to exhibiting antiangiogenic properties and suggest that the combination of these activities may provide a novel therapeutic approach for the treatment of AML.

IT **204005-46-9**, SU5416

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(the antiangiogenic protein kinase inhibitors SU5416 and SU6668 inhibit the SCF receptor (c-kit) in a human myeloid leukemia cell line and in acute myeloid leukemia blasts)

REFERENCE COUNT:

REFERENCE(S):

(1) Aguayo, A; Blood 1999, V94, P3717 HCAPLUS

(3) Bellamy, W; Cancer Res 1999, V59, P728 HCAPLUS (4) Bene, M; Blood 1998, V92, P596 HCAPLUS

(6) Chabot, B; Nature 1988, V335, P88 HCAPLUS(7) Dias, S; J Clin Invest 2000, V106, P511 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

2001:96419 HCAPLUS

DOCUMENT NUMBER:

135:116407

TITLE:

Zebrafish angiogenesis: A new model for drug screening

AUTHOR(S):

Serbedzija, George N.; Flynn, Edward; Willett,

Catherine E.

CORPORATE SOURCE:

Phylonix Pharmaceuticals, Inc., Cambridge, MA, 02139,

USA

SOURCE:

Angiogenesis (2000), Volume Date 1999, 3(4), 353-359

CODEN: AGIOFT; ISSN: 0969-6970

PUBLISHER:

Kluwer Academic Publishers

DOCUMENT TYPE: LANGUAGE:

Journal English

Angiogenesis is necessary for tumor growth, making inhibition of vessel formation an excellent target for cancer therapy. Current assays for angiogenesis, however, are too complex to be practical for drug screening. Here, we demonstrate that the zebrafish is a viable whole animal model for screening small mols. that affect blood vessel formation. Blood vessel patterning is highly characteristic in the developing zebrafish embryo and the subintestinal vessels (SIVs) can be stained and visualized microscopically as a primary screen for compds. that affect angiogenesis. Small mols. added directly to the fish culture media diffuse into the embryo and induce observable, dose-dependent effects. To evaluate the zebrafish as a model, we used two angiogenesis inhibitors, SU5416 and TNP470, both of which have been tested in mammalian systems. Both compds. caused a redn. in vessel formation when introduced to zebrafish embryos prior to the onset of angiogenesis. Short duration (1 h) exposure of SU5416 was sufficient to block new angiogenic and vasculogenic vessel formation. In contrast, TNP470 required continuous exposure to block SIV formation and had no apparent effect on vasculogenic vessel formation. ascertain whether blood vessels in the zebrafish embryo respond to angiogenic compds., we introduced human VEGF into embryos. Injection of VEGF caused an observable increase in SIV formation.

ΙT **204005-46-9**, SU5416

RL: BAC (Biological activity or effector, except adverse); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (zebrafish angiogenesis: a model for drug screening)

REFERENCE COUNT:

22

REFERENCE(S):

- (2) Bergers, G; Science 1999, V284, P808 HCAPLUS
- (3) Detrich, H; Proc Natl Acad Sci USA 1995, V92, P10713 HCAPLUS
- (4) Drake, C; Proc Natl Acad Sci USA 1995, V92, P7657 **HCAPLUS**
- (5) D'Amore, P; Angiogenesis Sci Med 1999, P44 HCAPLUS
- (6) Ferrara, N; Endocr Rev 1997, V18, P4 HCAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

2001:83373 HCAPLUS

DOCUMENT NUMBER:

135:86674

TITLE:

The angiogenesis inhibitor SU5416 has long-lasting

effects on vascular endothelial growth factor receptor

phosphorylation and function

AUTHOR(S):

Mendel, Dirk B.; Schreck, Randall E.; West, David C.; Li, Guangmin; Strawn, Laurie M.; Tanciongco, Sheila S.; Vasile, Stefan; Shawver, Laura K.; Cherrington,

Julie M.

CORPORATE SOURCE:

Sugen, Inc., South San Francisco, CA, 94080, USA

SOURCE:

Clin. Cancer Res. (2000), 6(12), 4848-4858

CODEN: CCREF4; ISSN: 1078-0432

PUBLISHER:

American Association for Cancer Research

DOCUMENT TYPE:

Journal

LANGUAGE: English

SU5416, a selective inhibitor of the tyrosine kinase activity of the vascular endothelial growth factor (VEGF) receptor Flk-1/KDR, is currently in Phase III clin. trials for the treatment of advanced malignancies. In cellular assays, SU5416 inhibits the VEGF-dependent mitogenic/proliferative response of human umbilical vein endothelial cells (HUVECs). In tumor xenograft models, SU5416 inhibits the growth of tumors from a variety of origins by inhibiting tumor angiogenesis. In three different human tumor xenograft models, infrequent (once or twice a week) administration of SU5416 is efficacious despite the fact that it has a short plasma half-life (30 min), which suggests that SU5416 has long-lasting inhibitory activity in vivo. The goal of the present study was to det. the basis for the prolonged activity of SU5416. The results indicate that a short (3 h) exposure to 5 .mu.M SU5416 (to mimic plasma levels of the compd. as measured in patients who were receiving SU5416 therapy) produced long-lasting (at least 72 h) inhibition of the VEGF-dependent proliferation of HUVECs in culture, which indicate that SU5416 has long-lasting inhibitory activity in vitro as well as in vivo. SU5416 treatment of HUVECs did not affect surface expression of Flk-1/KDR or the affinity of the receptor for VEGF. Instead, the durability of the in vitro activity of SU5416 was shown to be attributable to its long-lasting ability to specifically inhibit VEGF-dependent phosphorylation of Flk-1/KDR and subsequent downstream signaling, although SU5416 is not an irreversible inhibitor of Flk-1/KDR tyrosine kinase The long-lasting inhibition of cellular responses to VEGF was attributable to the accumulation of SU5416 in cells, as shown using radiolabeled compd., such that inhibitory cellular concns. of SU5416 are maintained long after the removal of the compd. from the medium. The long-lasting inhibitory activity of SU5416 in vitro is consistent with the finding that SU5416 has demonstrated evidence of biol. activity in clin. studies when administered twice a week despite a short plasma half-life.

ΙT 204005-46-9, SU5416

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (angiogenesis inhibitor SU5416 has long-lasting effects on

vascular endothelial growth factor receptor phosphorylation and function in relation to antitumor effects)

REFERENCE COUNT:

48

REFERENCE(S):

- (2) Asano, M; Cancer Res 1995, V55, P5296 HCAPLUS
- (5) Bridges, A; Curr Med Chem 1999, V6, P825 HCAPLUS
- (6) Cherrington, J; Adv Cancer Res 2000, V79, P1 **HCAPLUS**
- (7) Claffey, K; Cancer Res 1996, V56, P172 HCAPLUS
- (9) Discafani, C; Biochem Pharmacol 1999, V57, P917 **HCAPLUS**

ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2001 ACS L14 ANSWER 5 OF 16 2000:860816 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 134:141334

Biotransformation of the anti-angiogenic compound TITLE:

AUTHOR(S): Antonian, Lida; Zhang, Hongbing; Yang, Cheng; Wagner,

Greq; Shawver, Laura K.; Shet, Manjunath; Ogilvie,

Brian; Madan, Ajay; Parkinson, Andrew

SUGEN, Inc., South San Francisco, CA, 94080, USA CORPORATE SOURCE:

Drug Metab. Dispos. (2000), 28(12), 1505-1512 SOURCE:

CODEN: DMDSAI; ISSN: 0090-9556

American Society for Pharmacology and Experimental PUBLISHER:

Therapeutics

DOCUMENT TYPE: Journal English LANGUAGE:

SU5416 [3-(3,5-dimethyl-1H-pyrrol-2-ylmethylene)-1,3-dihydro-indol-2-one], an inhibitor of VEGF (vascular endothelial growth factor) receptor tyrosine kinase, Flk-1/KDR (fetal liver kinase 1/kinase insert domain-contg. receptor), also known as VEGF receptor 2 (VEGFR2) is in advanced clin. trials for treatment of AIDS-related Kaposi's sarcoma and colorectal and nonsmall cell lung cancers. Since this chem. class has not been studied previously with therapeutic intent, the present study was designed to investigate the in vitro metab. of SU5416 by mouse, rat, dog, monkey, and human liver microsomes and to identify the major metabolites of SU5416. An HPLC procedure was developed and validated to resolve and quantify SU5416 and its metabolites. To evaluate the in vitro metab. of SU5416, pooled liver microsomes from mice, rats, dogs, monkeys, and humans were incubated with SU5416 (25 .mu.M) in the presence of an NADPH-generating system. In the presence of NADPH, mouse, rat, dog, monkey, and human liver microsomes converted SU5416 to at least 12, 9, 9, 7, and 6 polar metabolites, resp. Microsomal metab. of SU5416 showed marked species differences in the levels of different metabolites formed. The overall rate of SU5416 metab. by liver microsomes from the species examd. followed the rank order: monkey .gtoreq. mouse .apprxeq. rat > dog > human. Two major metabolites of SU5416 were identified, a hydroxymethyl deriv. of SU5416 (M12) and a carboxylic acid deriv. of SU5416 (M6), by spectroscopic methods and comparison with authentic compds. Both of these oxidative metabolites were further metabolized in vivo through qlucuronidation. The metabolic fate of SU5416 in microsomes from various species as well as data from in vivo biotransformation in the rat are discussed.

IΤ **204005-46-9**, SU5416

RL: ANT (Analyte); BPR (Biological process); ANST (Analytical study); BIOL (Biological study); PROC (Process)

(biotransformation of anti-angiogenic compd. SU5416)

280748-38-1, SU 6689 280748-39-2, SU 6595 ΙT 280748-41-6, SU 9838 324047-04-3 324047-05-4

19

RL: MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative)

(biotransformation of anti-angiogenic compd. SU5416)

REFERENCE COUNT:

(1) Abulafia, O; Gynecol Oncol 1999, V72, P220 HCAPLUS REFERENCE(S):

(2) Cherrington, J; Adv Cancer Res 2000, V79, P1 **HCAPLUS**

- (5) Ferrara, N; J Mol Med 1999, V77, P527 HCAPLUS
- (6) Folkman, J; Nat Med 1995, V1, P27 HCAPLUS(7) Fong, T; Cancer Res 1999, V59, P99 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2001 ACS

2000:685884 HCAPLUS ACCESSION NUMBER:

133:308083 DOCUMENT NUMBER:

Inhibition of angiogenesis decreases alveolarization TITLE:

in the developing rat lung

Jakkula, Malathi; Le Cras, Timothy D.; Gebb, Sarah; AUTHOR(S):

Hirth, K. Peter; Tuder, Rubin M.; Voelkel, Norbert F.;

Abman, Steven H.

Pediatric Pulmonary Medicine, Pediatric Heart Lung CORPORATE SOURCE:

Center, Department of Pediatrics, University of Colorado School of Medicine, Denver, CO, 80218, USA

Am. J. Physiol. (2000), 279(3, Pt. 1), L600-L607 SOURCE:

CODEN: AJPHAP; ISSN: 0002-9513

American Physiological Society PUBLISHER:

DOCUMENT TYPE: Journal LANGUAGE: English

To det. whether angiogenesis is necessary for normal alveolarization, the authors studied the effects of two antiangiogenic agents, thalidomide and fumagillin, on alveolarization during a crit. period of lung growth in infant rats. Newborn rats were treated with daily injections of fumagillin, thalidomide, or vehicle during the first 2 wk of life. Compared with control treatment, fumagillin and thalidomide treatment reduced lung wt.-to-body wt. ratio and pulmonary arterial d. by 20 and 36%, resp., and reduced alveolarization by 22%. Because these drugs potentially have nonspecific effects on lung growth, the authors also studied the effects of Su-5416, an inhibitor of the vascular endothelial growth factor receptor known as kinase insert domain-contg. receptor/fetal liver kinase (KDR/flk)-1. As obsd. with the other antiangiogenic agents, Su-5416 treatment decreased alveolarization and arterial d. The authors conclude that treatment with three different antiangiogenic agents attenuated lung vascular growth and reduced alveolarization in the infant The authors speculate that angiogenesis is necessary for alveolarization during normal lung development and that injury to the developing pulmonary circulation during a crit. period of lung growth can contribute to lung hypoplasia.

204005-46-9, Su-5416 ΙΤ

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study) (antiangiogenic treatment decreases alveolarization in developing rat lung)

REFERENCE COUNT:

51

(2) Acarrequi, M; Am J Respir Cell Mol Biol 1999, V20, REFERENCE(S): P14 HCAPLUS

(3) Babaei, S; Circ Res 1998, V82, P1007 HCAPLUS

(4) Beck, L; FASEB J 1997, V11, P365 HCAPLUS

(5) Blanco, L; Am J Physiol Lung Cell Mol Physiol 1989, V257, PL240 HCAPLUS

(12) DeMello, D; Am J Respir Cell Mol Biol 1997, V16, P568 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2001 ACS 2000:509842 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 133:348326

Targeting angiogenesis inhibits tumor infiltration and TITLE:

expression of the pro-invasive protein SPARC

Vajkoczy, Peter; Menger, Michael D.; Goldbrunner, AUTHOR(S): Roland; Ge, Shugang; Annie, T.; Fong, T.; Vollmar,

Brigitte; Schilling, Lothar; Ullrich, Axel; Hirth, K. Peter; Tonn, Jorq C.; Schmiedek, Peter; Rempel, Sandra

CORPORATE SOURCE:

Department of Neurosurgery. Klinikum Mannheim,

University of Heidelberg, Mannheim, D-68167, Germany

SOURCE:

Int. J. Cancer (2000), 87(2), 261-268
CODEN: IJCNAW; ISSN: 0020-7136

PUBLISHER:

Wiley-Liss, Inc.

DOCUMENT TYPE: Journal LANGUAGE: English

The solid growth of high-grade glioma appears to be critically dependent on tumor angiogenesis. It remains unknown, however, whether the diffuse infiltration of glioma cells into healthy adjacent tissue is also dependent on the formation of new tumor vessels. Here, the authors analyze the relation between tumor angiogenesis and tumor cell infiltration in an exptl. glioma model. C6 cells were implanted into the dorsal skinfold chamber of nude mice, and tumor angiogenesis was monitored by intravital fluorescence videomicroscopy. Glioma infiltration was assessed by the extent of tumor cell invasion into the adjacent chamber tissue and by expression of SPARC, a cellular marker of glioma invasiveness. To test the hypothesis that glioma angiogenesis and glioma infiltration are codependent, the authors assessed tumor infiltration in both the presence and the absence of the angiogenesis inhibitor SU5416. SU5416 is a selective inhibitor of the VEGF/Flk-I signal-transduction pathway, a crit. pathway implicated in angiogenesis. Control tumors $\ \, \text{demonstrated both high angiogenic activity and tumor cell invasion}$ accompanied by strong expression of SPARC in invading tumor cells at the tumor-host tissue border. SU5416-treated tumors demonstrated reduced vascular d. and vascular surface in the tumor periphery accompanied by marked inhibition of glioma invasion and decreased SPARC expression. A direct effect of SU5416 on glioma cell motility and invasiveness was excluded by in vitro migration and invasion assays. These results suggest a crucial role for glioma-induced angiogenesis as a prerequisite for diffuse tumor invasion and a possible therapeutic role for anti-angiogenic compds. as inhibitors of both solid and diffuse infiltrative tumor growth.

204005-46-9, SU5416 IT

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (targeting angiogenesis inhibits tumor infiltration and expression of pro-invasive protein SPARC using VEGF/Flk-I signal-transduction pathway inhibitor SU5416)

REFERENCE COUNT:

21

REFERENCE(S):

- (2) Brooks, P; Cell 1994, V79, P1157 HCAPLUS
- (4) Fong, T; Cancer Res 1999, V59, P99 HCAPLUS
- (6) Kupprion, C; J Biol Chem 1998, V273, P29635 **HCAPLUS**
- (9) Millauer, B; Nature (Lond) 1994, V367, P576 **HCAPLUS**
- (10) Murphy-Ullrich, J; J Cell Biochem 1995, V57, P341 **HCAPLUS**

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2001 ACS 2000:459469 HCAPLUS ACCESSION NUMBER:

133:144316 DOCUMENT NUMBER:

Development of SU5416, a selective small molecule TITLE:

inhibitor of VEGF receptor tyrosine kinase activity,

as an anti-angiogenesis agent

Mendel, Dirk B.; Laird, A. Douglas; Smolich, Beverly AUTHOR(S):

D.; Blake, Robert A.; Liang, Congxin; Hannah, Alison L.; Shaheen, Raymond M.; Ellis, Lee M.; Weitman, Steve; Shawver, Laura K.; Cherrington, Julie M. SUGEN, Inc., South San Francisco, CA, 94080, USA Anti-Cancer Drug Des. (2000), 15(1), 29-41

CODEN: ACDDEA; ISSN: 0266-9536

PUBLISHER: Oxford University Press
DOCUMENT TYPE: Journal; General Review

LANGUAGE: English

AB A review with over 60 refs. Angiogenesis, or the sprouting of new blood vessels, is a central process in the growth of solid tumors. For many cancers, the extent of vascularization of a tumor is a neg. prognostic indicator signifying aggressive disease and increased potential for metastasis. Recent efforts to understand the mol. basis of tumor-assocd. angiogenesis have identified several potential therapeutic targets, including the receptor tyrosine kinases for the angiogenic factor vascular endothelial growth factor (VEGF). Here we review the approach taken at SUGEN, Inc. to discover and develop small mol. inhibitors of receptor tyrosine kinases as anti-angiogenic agents. We focus on SU5416, a selective inhibitor of VEGF receptors that is currently in clin. development for the treatment of advanced malignancies. Its biochem., biol. and pharmacol. properties are reviewed and clin. implications discussed.

IT **204005-46-9**, SU5416

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (VEGF receptor tyrosine kinase inhibitors SU5416 development as anti angiogenesis agent)

REFERENCE COUNT:

CORPORATE SOURCE:

SOURCE:

60

REFERENCE(S):

(1) Adnane, J; Oncogene 1991, V6, P659 HCAPLUS

- (2) Albini, A; Nature Medicine 1996, V2, P1371 HCAPLUS
- (3) Angelov, L; Cancer Research 1999, V59, P5536 HCAPLUS
- (5) Armesilla, A; Molecular and Cellular Biology 1999, V19, P2032 HCAPLUS
- (6) Bais, C; Nature 1998, V391, P86 HCAPLUS ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 2000:417312 HCAPLUS

DOCUMENT NUMBER:

2000:41/312 HCAPLU 133:159618

TITLE:

AUTHOR(S):

Identification of Substituted 3-[(4,5,6,7-Tetrahydro-1H-indol-2-yl)methylene]-1,3-dihydroindol-2-ones as

Growth Factor Receptor Inhibitors for VEGF-R2

(Flk-1/KDR), FGF-R1, and PDGF-R.beta. Tyrosine Kinases Sun, Li; Tran, Ngoc; Liang, Congxing; Hubbard, Steve; Tang, Flora; Lipson, Kenneth; Schreck, Randall; Zhou,

Yong; McMahon, Gerald; Tang, Cho

CORPORATE SOURCE: SUGEN Inc., South San Francisco, CA, 94080-4811, USA

SOURCE: J. Med. Chem. (2000), 43(14), 2655-2663

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal LANGUAGE: English

AB A series of new 3-substituted indolin-2-ones contg. a tetrahydroindole moiety was developed as specific inhibitors of receptor tyrosine kinases assocd. with VEGF-R, FGF-R, and PDGF-R growth factor receptors. These compds. were evaluated for their inhibitory properties toward VEGF-R2 (Flk-1/KDR), FGF-R1, PDGF-R.beta., p60c-Src, and EGF-R tyrosine kinases and their ability to inhibit growth factor-dependent cell proliferation.

Structure-activity relationships of this new pharmacophore have been detd. at the level of kinase inhibition. Compds. contg. a propionic acid moiety at the C-3' position of the tetrahydroindole ring represented the most potent indolin-2-ones to inactivate the VEGF, FGF, and PDGF receptor kinases. The inhibitory activities of 3-[3-(2-carboxyethyl)-4,5,6,7tetrahydro-1H-indol-2-ylmethylene]-2-oxo-2,3-dihydro-1H-indole-5carboxylic acid against VEGF-R2 (Flk-1), 3-{2-[6-(2-methoxyphenyl)-2-oxo-1,2-dihydroindol-3-ylidenemethyl]-4,5,6,7-tetrahydro-1H-indol-3-yl}propionic acid against FGF-R1, and 3-[2-(5-bromo-2-oxo-1,2-dihydroindol-3-ylidenemethyl)-4,5,6,7-tetrahydro-1H-indol-3-yl]propionic acid (I) against PDGF-R.beta. were 4, 80, and 4 nM, resp. However, all of these compds. were inactive when tested against the EGF-R tyrosine kinase. Compds. $3-[2-(2-\infty -1, 2-\text{dihydroindol}-3-\text{ylidenemethyl})-4, 5, 6, 7-\text{tetrahydro-}$ 1H-indol-3-yl]propionic acid (II) and I represented the most potent inhibitors of these classes to inhibit both biochem. kinase and growth factor-dependent cell proliferation for these three targets. In addn., compd. II was cocrystd. with the catalytic domain of FGF-R1 providing evidence to explain the structure-activity relation results. This study has provided evidence to support the potential of these new tyrosine kinase inhibitors for the treatment of angiogenesis and other growth factor-related diseases including human cancers. 204005-46-9, Su5416 215543-92-3

IT

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(substituted [(tetrahydroindolyl)methylene]dihydroindolones as growth factor receptor inhibitors for VEGF-R2 (Flk-1/KDR) and FGF-R1, and PDGF-R.beta. tyrosine kinases and as inhibitors of growth factor-dependent cell proliferation)

288144-28-5P IT

> RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

(substituted [(tetrahydroindolyl)methylene]dihydroindolones as growth factor receptor inhibitors for VEGF-R2 (Flk-1/KDR) and FGF-R1, and PDGF-R.beta. tyrosine kinases and as inhibitors of growth factor-dependent cell proliferation)

288144-19-4P 288144-20-7P 288144-21-8P

288144-22-9P 288144-23-0P 288144-24-1P

288144-25-2P 288144-26-3P 288144-27-4P

288144-29-6P 288144-30-9P 288144-31-0P

288144-32-1P 288144-33-2P 288144-34-3P

17

288144-35-4P 288144-36-5P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(substituted [(tetrahydroindolyl)methylene]dihydroindolones as growth factor receptor inhibitors for VEGF-R2 (Flk-1/KDR) and

FGF-R1, and PDGF-R.beta. tyrosine kinases and as inhibitors of growth factor-dependent cell proliferation)

REFERENCE COUNT:

REFERENCE(S):

- (3) Folkman, J; J Biol Chem 1992, V267, P10931 HCAPLUS
- (6) Hanahan, D; Cell 1996, V86, P353 HCAPLUS
- (10) Mohammadi, M; Cell 1996, V86, P577 HCAPLUS
- (11) Mohammadi, M; Science 1997, V276, P955 HCAPLUS
- (12) Otwinowski, Z; Methods Enzymol 1997, V276, P307 **HCAPLUS**

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 2000:144722 HCAPLUS

132:185454 DOCUMENT NUMBER: Use of anti-angiogenic agents for inhibiting vessel TITLE: wall injury Brown, Charles L., III; Gorlin, Steve INVENTOR(S): Global Vascular Concepts, Inc., USA PATENT ASSIGNEE(S): SOURCE: PCT Int. Appl., 29 pp. CODEN: PIXXD2 DOCUMENT TYPE: Patent LANGUAGE: English FAMILY ACC. NUM. COUNT: PATENT INFORMATION: DATE . PATENT NO. KIND APPLICATION NO. DATE ______ ____ -----______ WO 1999-US19218 19990824 20000302 WO 2000010552 Α2 WO 2000010552 А3 20001123 AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 9956871 20000314 AU 1999-56871 19990824 A1 US 1998-97579 P 19980824 PRIORITY APPLN. INFO.: WO 1999-US19218 W 19990824 Use of anti-angiogenic agents to inhibit an undesirable response to vessel AB wall injury, including stent neointima, dialysis graft neointima, vascular graft-induced neointima, and the treatment of benign hypertrophic scar formation as well as the treatment and passivation of unstable atherosclerotic plaques are provided. The invention provides for the use of catheter-based devices for enhancing the local delivery of anti-angiogenic agents into the endothelial tissues of blood vessels of the living body. 204005-46-9, SU5416 ΙT RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (anti-angiogenic agents for inhibiting vessel wall injury) L14 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 2000:117816 HCAPLUS DOCUMENT NUMBER: 133:37825 Inhibition of tumor growth, angiogenesis, and TITLE: microcirculation by the novel Flk-1 inhibitor SU5416 as assessed by intravital multifluorescence videomicroscopy Vajkoczy, Peter; Menger, Michael D.; Vollmar, AUTHOR(S): Brigitte; Schilling, Lothar; Schmiedek, Peter; Hirth, K. Peter; Ullrich, Axel; Fong, T. Annie T. Department of Neurosurgery, Klinikum Mannheim, CORPORATE SOURCE: University of Heidelberg, Mannheim, D-68167, Germany Neoplasia (N. Y.) (1999), 1(1), 31-41 SOURCE: CODEN: NEOPFL; ISSN: 1522-8002 Stockton Press PUBLISHER:

AB Vascular endothelial growth factor (VEGF) plays a fundamental role in mediating tumor angiogenesis and tumor growth. The direct effect of

Journal

English

DOCUMENT TYPE: LANGUAGE:

SU5416, a novel small-mol. inhibitor of the Flk-1-mediated signal transduction pathway of VEGF, on tumor angiogenesis and microhemodynamics of an exptl. glioblastoma was investigated by intravital multifluorescence videomicroscopy. SU5416 treatment suppressed tumor growth. In parallel, SU5416 demonstrated a potent antiangiogenic activity, resulting in redn. of both the total and functional vascular d. of the tumor microvasculature, which indicates an impaired vascularization as well as perfusion failure in the treated tumors. This malperfusion was not compensated for by changes in vessel diam. or recruitment of nonperfused vessels. Analyses of the tumor microcirculation revealed microhemodynamic changes after angiogenesis blockade, such as a higher red cell velocity and blood flow in remnant tumor vessels than in controls. The results demonstrate that the novel antiangiogenic concept of targeting the tyrosine kinase of Flk-1/KDR by means of a small-mol. inhibitor represents an efficient strategy for controlling growth and progression of angiogenesis-dependent tumors.

IT 204005-46-9, SU 5416

RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(inhibition of glioblastoma growth, angiogenesis, and microcirculation by tyrosine kinase inhibitor SU5416)

REFERENCE COUNT:

·25

REFERENCE(S):

- (1) Abramovitch, R; Cancer Res 1995, V55, P1956 HCAPLUS
- (2) Andrade, S; Br J Pharmacol 1992, V107, P1092 HCAPLUS
- (5) Boucher, Y; Cancer Res 1996, V56, P4264 HCAPLUS
- (6) Brogi, E; J Clin Invest 1996, V97, P469 HCAPLUS
- (7) Cheng, S; Proc Natl Acad Sci USA 1996, V93, P8502 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1999:725101 HCAPLUS

DOCUMENT NUMBER:

132:30444

TITLE:

Inhibition of angiogenesis by blocking activation of the vascular endothelial growth factor receptor 2 leads to decreased growth of neurogenic sarcomas

AUTHOR(S):

Angelov, Lilyana; Salhia, Bodour; Roncari, Luba;

McMahon, Gerald; Guha, Abhijit

CORPORATE SOURCE:

Division of Neurosurgery, Toronto Western Hospital, University of Toronto, Toronto, ON, M5T 2S8, Can.

SOURCE: Cancer Res. (1999), 59(21), 5536-5541

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: AACR Subscription Office

DOCUMENT TYPE: Journal LANGUAGE: English

AB Neurogenic sarcomas are incurable, common malignant human peripheral nerve tumors subject to local recurrence and systemic metastasis. In this study, the vascularity, vascular endothelial growth factor (VEGF) expression, and effects of inhibiting VEGF receptor on growth of neurogenic sarcomas were examd. Vascularization and VEGF expression were 6.4- and 15-fold higher in tumors than in normal nerves. The small mol. inhibitor (SU5416) of VEGF receptor 2 had no effect on neurogenic sarcoma cell lines in vitro, but the growth of a human tumor explant xenograft model was reduced by 54.8% compared to vehicle. Redn. in tumor growth was due to decreased tumor angiogenesis, leading to redn. of tumor cell proliferation and increased apoptosis. Inhibiting VEGF function may therefore be a useful adjuvant therapy for neurogenic sarcomas.

ΙT 204005-46-9, SU5416

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(angiogenesis inhibition by VEGF2 blocking leads to decreased growth of neurogenic sarcomas)

REFERENCE COUNT:

69

REFERENCE(S):

- (1) Adamis, A; Biochem Biophys Res Commun 1993, V193, P631 HCAPLUS
- (2) Alon, T; Nat Med 1995, V1, P1024 HCAPLUS
- (5) Basu, T; Nature 1992, V356, P713 HCAPLUS
- (6) Brown, L; Cancer Res 1993, V53, P4727 HCAPLUS
- (7) Cawthon, R; Cell 1990, V62, P193 HCAPLUS
- ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1999:725076 HCAPLUS

DOCUMENT NUMBER:.

132:44604

TITLE:

Antiangiogenic therapy targeting the tyrosine kinase receptor for vascular endothelial growth factor receptor inhibits the growth of colon cancer liver metastasis and induces tumor and endothelial cell

apoptosis

AUTHOR(S):

Shaheen, Raymond M.; Davis, Darren W.; Liu, Wenbiao; Zebrowski, Brian K.; Wilson, Michael R.; Bucana, Corazon D.; McConkey, David J.; McMahon, Gerald; Ellis, Lee M.

CORPORATE SOURCE:

Departments of Surgical Oncology, Anderson Cancer Center, The University of Texas M. D., Houston, TX,

77030, USA

SOURCE:

Cancer Res. (1999), 59(21), 5412-5416

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER:

AACR Subscription Office

DOCUMENT TYPE:

Journal

LANGUAGE: English

Increased vascular endothelial growth factor (VEGF) expression is assocd. with colon cancer metastases. We hypothesized that inhibition of VEGF receptor activity could inhibit colon cancer liver metastases. BALB/c mice underwent splenic injection with CT-26 colon cancer cells to generate metastases. Mice received daily i.p. injections of vehicle, tyrosine kinase inhibitor for Flk-1/KDR (SU5416) or tyrosine kinase inhibitor for VEGF, basic fibroblast growth factor, and platelet-derived growth factor receptors (SU6668). SU5416 and SU6668 resp. inhibited metastases (48.1% and 55.3%), microvessel formation (42.0% and 36.2%), and cell proliferation (24.4% and 27.3%) and increased tumor cell (by 2.6- and 4.3-fold) and endothelial cell (by 18.6- and 81.4-fold) apoptosis (P < VEGF receptor inhibitors increased endothelial cell apoptosis, suggesting that VEGF may serve as an endothelial survival factor.

IT 204005-46-9, SU 5416

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antiangiogenic therapy targeting VEGF receptor tyrosine

kinase inhibits liver metastasis of colon cancer and induces tumor and endothelial cell apoptosis)

REFERENCE COUNT:

REFERENCE(S):

(1) Bussolino, F; Trends Biochem Sci 1997, V22, P251 **HCAPLUS**

- (2) Dong, Z; J Natl Cancer Inst 1994, V86, P913 HCAPLUS
- (3) Folkman, J; Nat Med 1995, V1, P27 HCAPLUS

(5) Fong, T; Cancer Res 1999, V59, P99 HCAPLUS

(6) Gerber, H; J Biol Chem 1998, V273, P13313 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2001 ACS L14 ANSWER 14 OF 16

ACCESSION NUMBER:

1999:65738 HCAPLUS

DOCUMENT NUMBER:

130:246450

TITLE:

SU5416 is a potent and selective inhibitor of the

vascular endothelial growth factor receptor

(Flk-1/KDR) that inhibits tyrosine kinase catalysis, tumor vascularization, and growth of multiple tumor

types

AUTHOR(S):

Fong, T. Annie T.; Shawver, Laura K.; Sun, Li; Tang, Cho; App, Harald; Powell, T. Jeff; Kim, Young H.; Schreck, Randall; Wang, Xueyan; Risau, Werner; Ullrich, Axel; Hirth, K. Peter; McMahon, Gerald SUGEN, Inc., South San Francisco, CA, 94080, USA

CORPORATE SOURCE:

Cancer Res. (1999), 59(1), 99-106

SOURCE:

CODEN: CNREA8; ISSN: 0008-5472

AACR Subscription Office PUBLISHER:

DOCUMENT TYPE: Journal LANGUAGE: English

SU5416, a novel synthetic compd., is a potent and selective inhibitor of the Flk-1/KDR receptor tyrosine kinase that is presently under evaluation in Phase I clin. studies for the treatment of human cancers. SU5416 was shown to inhibit vascular endothelial growth factor-dependent mitogenesis of human endothelial cells without inhibiting the growth of a variety of tumor cells in vitro. In contrast, systemic administration of SU5416 at nontoxic doses in mice resulted in inhibition of s.c. tumor growth of cells derived from various tissue origins. The antitumor effect of SU5416 was accompanied by the appearance of pale white tumors that were resected from drug-treated animals, supporting the antiangiogenic property of this agent. These findings support that pharmacol. inhibition of the enzymic activity of the vascular endothelial growth factor receptor represents a novel strategy for limiting the growth of a wide variety of tumor types.

ΙT 204005-46-9, SU 5416

> RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(SU5416: selective inhibitor of Flk-1/KDR receptor tyrosine kinase, tumor vascularization and growth)

REFERENCE COUNT:

REFERENCE(S):

- (2) Asano, M; Cancer Res 1995, V55, P5296 HCAPLUS
- (4) Brogi, E; Circulation 1994, V90, P649 HCAPLUS
- (5) Brown, L; Cancer Res 1993, V53, P4727 HCAPLUS
- (6) Bussolino, F; Trends Biochem Sci 1997, V22, P251 HCAPLUS
- (7) Carmeliet, P; Nature (Lond) 1996, V380, P435. **HCAPLUS**

ALL CITATIONS AVAILABLE IN THE RE FORMAT

L14 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1997:640690 HCAPLUS

DOCUMENT NUMBER:

127:314804

TITLE:

Assays for KDR/FLK-1 receptor tyrosine kinase

inhibitors, and use of the inhibitors for treatment of

vasculogenesis- and angiogenesis-related diseases Hirth, Klaus P.; McMahon, Gerald; Shawver, Laura K.

INVENTOR(S):

Sugen, Inc., USA

PATENT ASSIGNEE(S): SOURCE:

·PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

APPLICATION NO. DATE PATENT NO. KIND DATE ----______ ----_____ WO 9734920 A1 19970925 WO 1997-US3378 19970304 W: AL, AM, AU, AZ, BA, BB, BG, BR, BY, CA, CN, CU, CZ, EE, GE, GH, HU, IL, IS, JP, KG, KP, KR, KZ, LC, LK, LR, LT, LV, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG AU 1997-20667 AU 9720667 A1 19971010 19970304 US 1996-621734 PRIORITY APPLN. INFO.: 19960321 WO 1997-US3378 19970304

Processes are disclosed for the identification of compds. and ΑB pharmaceutical compns. capable of selectively and potently inhibiting KDR/FLK-1 tyrosine kinase signal transduction in order to inhibit vasculogenesis and/or angiogenesis. The invention also relates to compds. and compns. identified using the methods of the invention and the use thereof for the treatment of disease relating to inappropriate vasculogenesis and/or angiogenesis. The invention provides an assay cascade comprised of several "filter steps" of increasing selectivity which identify a limited subset of candidate compds. affecting the VEGF. receptor on the mol. level.

3359-49-7, SU 4928 5812-07-7, SU 4312 62540-08-3 ΙT , SU 5208 91822-51-4, SU 4314 186611-03-0, SU 4932 186611-55-2, SU 4313 204005-46-9, SU 5416 RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses) -(KDR/FLK-1 receptor tyrosine kinase inhibitor identification assay, and use of compds. for treatment of vasculogenesis- and angiogenesis-related diseases)

L14 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 1995:813058 HCAPLUS

DOCUMENT NUMBER: 123:208831

Biologically active 3-substituted oxindole derivatives TITLE:

useful as anti-angiogenic agents

Heath, William Francis Heat, Jr.; McDonald, John INVENTOR(S):

Hampton III; Brasca, Maria Gabriella; Orzi, Fabrizio;

Crugnola, Angelo; Ballinari, Dario; Mariani,

Mariangela

PATENT ASSIGNEE(S): Pharmacia S.P.A., Italy PCT Int. Appl., 104 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE WO 9517181 A1 19950629 WO 1994-EP3664 19941108 W: AU, BY, CA, HU, JP, KR, KZ, NO, PL, RU, UA

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PRIORITY APPLN. INFO.:
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                          MARPAT 123:208831
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OTHER SOURCE(S):

GΙ

AB Compds. I (Ar = naphthalene, tetralin, quinoline, isoquinoline, indole; n = 0 or an integer of 1 to 3; R1 = H, C1-6 alkyl, C2-6 alkanoyl; R2 = H, halogen, C1-6 alkyl, cyano, carboxy, nitro, NHR; R = H, C1-6 alkyl; R3 = HH, C1-6 alkyl; R4 = H, OH, C1-6 alkoxy, C2-6 alkanoyloxy, carboxy, nitro, NHR; R5 = H, C1-6 alkyl, halogen) or a pharmaceutically acceptable salt thereof are useful as angiogenesis inhibitors. Products contg. an angiogenesis inhibitor or a pharmaceutically acceptable salt thereof and an antitumor agent are used as a combined prepn. for anticancer therapy. A compn. (for 10,000 tablets) contg. 3-[(3'-hydroxy-2'-tetralyl)methylen]-2-oxindole 250. lactose 800, corn starch 415, talc 30 and Mg stearate 5 g, resp., was formulated.

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137478-39-8 137478-40-1 137479-10-8
137479-11-9 137479-12-0 137479-13-1
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137501-13-4 148563-43-3 148563-44-4
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149492-57-9 168121-37-7 168121-38-8
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168121-45-7 168121-46-8 168121-47-9
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168121-51-5 168121-52-6
RL: BAC (Biological activity or effector, except adverse); THU
(Therapeutic use); BIOL (Biological study); USES (Uses)
   (oxindole derivs. as anti-angiogenic agents)
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Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
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L15 ANSWER 1 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN **342808-38-2** REGISTRY

CN 2H-Indol-2-one, 3-[(2,3-difluorophenyl)methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

MF C15 H9 F2 N O

SR CA

LC STN Files: CA, CAPLUS

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE) 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:19497

L15 ANSWER 3 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN **324047-05-4** REGISTRY

CN .beta.-D-Glucopyranuronic acid, 1-[5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl-1H-pyrrole-2-carboxylate] (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C21 H20 N2 · O9

SR CA

LC STN Files: CA, CAPLUS, TOXLIT

Absolute stereochemistry.

Double bond geometry unknown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 134:141334

L15 ANSWER 5 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 288144-36-5 REGISTRY

CN 1H-Indole-3-propanoic acid, 2-[(Z)-[1,2-dihydro-6-(4-methoxyphenyl)-2-oxo-

3H-indol-3-ylidene]methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

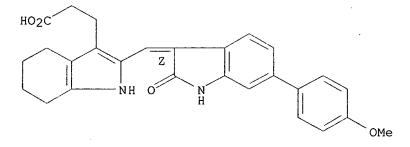
FS STEREOSEARCH

MF C27 H26 N2 O4

SR CA

LC STN Files: CA, CAPLUS, TOXLIT

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:159618

L15 ANSWER 10 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 288144-31-0 REGISTRY

CN 1H-Indole-3-propanoic acid, 2-[(Z)-(5-carboxy-1,2-dihydro-2-oxo-3H-indol-3-

ylidene)methyl]-4,5,6,7-tetrahydro- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C21 H20 N2 O5

SR CA

LC STN Files: CA, CAPLUS, TOXLIT

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:159618

L15 ANSWER 15 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 288144-26-3 REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-6-(2-methoxyphenyl)-3-[(4,5,6,7-tetrahydro-1H-indol-2-yl)methylene]-, (3Z)- (9CI) (CA INDEX NAME)

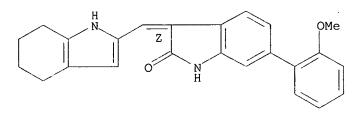
FS STEREOSEARCH

MF C24 H22 N2 O2

SR CA

LC STN Files: CA, CAPLUS, TOXLIT

Double bond geometry as shown.



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:159618

L15 ANSWER 23 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 280748-41-6 REGISTRY

2H-Indol-2-one, 1,3-dihydro-3-[[5-(hydroxymethyl)-3-methyl-1H-pyrrol-2-yl]methylene]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN SU 9838

FS 3D CONCORD

MF C15 H14 N2 O2

SR CA

LC STN Files: CA, CAPLUS, TOXLIT

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:107247

REFERENCE 2: 134:141334

REFERENCE 3: 133:84238

L15 ANSWER 26 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 215543-92-3 REGISTRY

CN 1H-Pyrrole-3-propanoic acid, 2-[(1,2-dihydro-2-oxo-3H-indol-3-

ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN SU 5402

FS 3D CONCORD

MF C17 H16 N2 O3

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, DRUGUPDATES, PHAR, TOXLIT, USPATFULL

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

7 REFERENCES IN FILE CA (1967 TO DATE)

7 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:56059

REFERENCE 2: 134:159784

REFERENCE 3: 133:246860

REFERENCE 4: 133:159618

REFERENCE 5: 132:166123

REFERENCE 6: 132:137242

REFERENCE 7: 130:3771

L15 ANSWER 27 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 204005-46-9 REGISTRY

CN 2H-Indol-2-one, 3-[(3,5-dimethyl-1H-pyrrol-2-yl)methylene]-1,3-dihydro-(9CI) (CA INDEX NAME)

OTHER NAMES:

CN SU 5416

FS 3D CONCORD

MF C15 H14 N2 O

SR CA

LC STN Files: BIOSIS, CA, CAPLUS, DRUGPAT, DRUGUPDATES, TOXLIT, USPATFULL

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

37 REFERENCES IN FILE CA (1967 TO DATE)

37 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:146994

REFERENCE 2: 135:116407

REFERENCE 3: 135:107247

REFERENCE 4: 135:86674

REFERENCE 5: 135:56059

REFERENCE 6: 135:2309

REFERENCE 7: 134:348057

REFERENCE 8: 134:324500

REFERENCE 9: 134:316158

REFERENCE 10: 134:242681

L15 ANSWER 28 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN **186611-55-2** REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-3-[[4-(1-methylethyl)phenyl]methylene]- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN SU 4313

MF C18 H17 N O

SR CA

LC STN Files: CA, CAPLUS, CHEMCATS, TOXLIT, USPATFULL

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)

5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 133:234344

REFERENCE 2: 130:237471

REFERENCE 3: 130:237470

REFERENCE 4: 127:314804

REFERENCE 5: 126:139901

L15 ANSWER 30 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 168121-52-6 REGISTRY

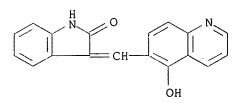
CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-hydroxy-6-quinolinyl)methylene]- (9CI)

(CA INDEX NAME)

MF C18 H12 N2 O2

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:208831

L15 ANSWER 46 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 149492-57-9 REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-3-(2-naphthalenylmethylene)- (9CI) (CA INDEX

NAME)

MF C19 H13 N O

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:208831

REFERENCE 2: 119:108407

L15 ANSWER 47 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 148563-59-1 REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-3-[(5-nitro-1H-indol-3-yl)methylene]- (9CI)

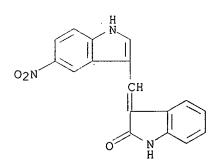
(CA INDEX NAME)

FS .3D CONCORD

MF C17 H11 N3 O3

SR CA

LC STN Files: CA, CAPLUS, CHEMCATS, TOXLIT, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:208831

REFERENCE 2: 119:49225

L15 ANSWER 64 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 137501-13-4 REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-3-(4-quinolinylmethylene)- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C18 H12 N2 O

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:208831

REFERENCE 2: 115:279621

L15 ANSWER 65 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 137479-21-1 REGISTRY

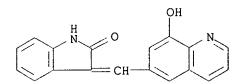
CN 2H-Indol-2-one, 1,3-dihydro-3-[(8-hydroxy-6-quinolinyl)methylene]- (9CI)

(CA INDEX NAME)

MF C18 H12 N2 O2

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:208831

REFERENCE 2: 115:279621

L15 ANSWER 72 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 137478-40-1 REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-3-(3-quinolinylmethylene)- (9CI) (CA INDEX NAME)

MF C18 H12 N2 O

SR CA

LC STN Files: CA, CAPLUS, TOXLIT, USPATFULL

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1967 TO DATE)

3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:208831

REFERENCE 2: 119:108407

REFERENCE 3: 115:279621

L15 ANSWER 75 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN **91822-51-4** REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-3-(1H-pyrrol-2-ylmethylene)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Indolinone, 3-(pyrrol-2-ylmethylene)- (7CI)

OTHER NAMES:

CN HA 12-16

CN SU 4314

FS 3D CONCORD

MF C13 H10 N2 O

LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, TOXLIT, USPATFULL (*File contains numerically searchable property data)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1967 TO DATE)

9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 133:234344

REFERENCE 2: 132:117566

REFERENCE 3: 131:254128

REFERENCE 4: 130:237471

REFERENCE 5: 130:237470

REFERENCE 6: 129:175549

REFERENCE 7: 128:204803

REFERENCE 8: 127:314804

REFERENCE 9: 126:139901

L15 ANSWER 76 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN **62540-08-3** REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-3-(2-thienylmethylene)- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN SU 5208

FS 3D CONCORD

MF C13 H9 N O S

LC STN Files: BEILSTEIN*, CA, CAPLUS, CHEMCATS, IFICDB, IFIPAT, IFIUDB,

TOXLIT, USPATFULL

(*File contains numerically searchable property data)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

9 REFERENCES IN FILE CA (1967 TO DATE)

9 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 130:252240

REFERENCE 2: 130:237471

REFERENCE 3: 130:237470

REFERENCE 4: 129:330650

REFERENCE 5: 129:216480

REFERENCE 6: 129:175549

REFERENCE 7: 127:314804

REFERENCE 8: 126:139901

REFERENCE 9: 86:171457

L15 ANSWER 77 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 55160-03-7 REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-3-(1-naphthalenylmethylene)- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H13 N O

LC STN Files: CA, CAPLUS, CHEMCATS, TOXLIT, USPATFULL

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:208831

REFERENCE 2: 82:139883

L15 ANSWER 78 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN **22813-84-9** REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-3-[(1-methyl-1H-indol-3-yl)methylene]- (9CI)

(CA INDEX NAME)

OTHER CA INDEX NAMES:
CN 2-Indolinone, 3-[(1-methylindol-3-yl)methylene]- (8CI)

FS 3D CONCORD

MF C18 H14 N2 O

LC STN Files: BEILSTEIN*, CA, CAPLUS, TOXLIT, USPATFULL

(*File contains numerically searchable property data)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)

4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:204803

REFERENCE 2: 123:208831

REFERENCE 3: 119:49225

REFERENCE 4: 71:3203

L15 ANSWER 79 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN **5812-07-7** REGISTRY

CN 2H-Indol-2-one, 3-[[4-(dimethylamino)phenyl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Indolinone, 3-[p-(dimethylamino)benzylidene]- (7CI, 8CI)

OTHER NAMES:

CN 3-(4-Dimethylaminobenzylidenyl)-2-indolinone

CN SU 4312

MF C17 H16 N2 O

LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CHEMCATS, TOXLIT, USPATFULL

(*File contains numerically searchable property data)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1967 TO DATE)

13 REFERENCES IN FILE CAPLUS (1967 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 133:234344

REFERENCE 2: 130:348928

REFERENCE 3: 130:252240

REFERENCE 4: 130:237471

REFERENCE 5: 130:237470

REFERENCE 6: 130:149064

REFERENCE 7: 129:330650

REFERENCE 8: 129:175549

REFERENCE 9: 127:314804

REFERENCE 10: 126:139901

L15 ANSWER 80 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 3367-88-2 REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-3-(2-pyridinylmethylene)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Indolinone, 3-(2-pyridylmethylene)- (7CI, 8CI)

FS 3D CONCORD

MF C14 H10 N2 O

LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CHEMCATS, CHEMINFORMRX, IFICDB, IFIPAT, IFIUDB, USPATFULL (*File contains numerically searchable property data)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1967 TO DATE)

4 REFERENCES IN FILE CAPLUS (1967 TO DATE)

3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 135:19497

REFERENCE 2: 127:190643

REFERENCE 3: 123:169529

REFERENCE 4: 86:171457

L15 ANSWER 81 OF 81 REGISTRY COPYRIGHT 2001 ACS

RN 3359-49-7 REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-3-(phenylmethylene)- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Indolinone, 3-benzylidene- (7CI, 8CI)

CN Oxindole, 3-benzylidene- (6CI)

OTHER NAMES:

CN 1,3-Dihydro-3-(phenylmethylene)-2H-indol-2-one

CN 3-Benzylidene-2-indolinone

CN SU 4928

MF C15 H11 N O

LC STN Files: BEILSTEIN*, CA, CAOLD, CAPLUS, CHEMCATS, IFICDB, IFIPAT, IFIUDB, TOXLIT, USPATFULL

(*File contains numerically searchable property data)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

18 REFERENCES IN FILE CA (1967 TO DATE)
18 REFERENCES IN FILE CAPLUS (1967 TO DATE)

6 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

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REFERENCE 7: 127:314804

REFERENCE 8: 126:139901

REFERENCE 9: 115:8574

REFERENCE 10: 112:98408 => fil hcaplus
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FILE COVERS 1947 - 16 Oct 2001 VOL 135 ISS 17 FILE LAST UPDATED: 15 Oct 2001 (20011015/ED)

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This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

HCAplus now provides online access to patents and literature covered in CA from 1947 to the present. On April 22, 2001, bibliographic information and abstracts were added for over 2.2 million references published in CA from 1947 to 1966.

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L18 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 2001:661426 HCAPLUS

DOCUMENT NUMBER: 135:226880

TITLE: Synthesis of Pyrolyllactone-indolinone derivatives as

kinase inhibitors

INVENTOR(S): Tang, Peng Cho; Miller, Todd A.; Li, Xiaoyuan; Zhang,

Ruofei; Cui, Jingrong; Huang, Ping; Wei, Chung Chen

PATENT ASSIGNEE(S): Sugen, Inc., USA

SOURCE: PCT Int. Appl., 148 pp. CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

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PATENT NO.
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                                                            DATE
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    WO 2001064681
                      A2
                                           WO 2001-US6214
                                                            20010228
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             MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ,
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             MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                        US 2000-185536
                                                        P 20000228
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* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [R1 = H, alkyl, (hetero)arom. ring, (hetero)aliph. ring, etc.; R2-5 = H, alkyl, (hetero)arom. ring, (hetero)aliph. ring; A, B, D, E = C or N provided that one or two = N and provided that when A, B, D or E = N, no R1 is attached to A, B, D or E; m = 2 - 4; q = 1 - 4] were prepd. Examples include data for over 50 compds. synthesized and over 20 bioassays (data for 4 bioassays provided). For instance, tosylmethyl isocyanide was added to 5,6-dihydro-2H-pyran-2-one (DBU, THF, 0.degree.C, room temp., 2 h.) to give 6,7-dihydro-2H-pyrano[3,4-c]pyrrol-4-one. This intermediate was formylated in the 1-position (DMF, POC13, DCM, room temp.; 1 h.) followed by condensation of the 1-formyl deriv. with 2-oxo-2,3-dihydro-1H-indole-5-sulfonic acid N-Me amide to yield II. II had IC50 = 0.005 mM for cdk2/cyclin A and IC50 = 6.64 mM for GST-Flk1. Compds. II are used to treat cancer, e.g., squamous cell carcinoma, astrocytoma, Kaposi's sarcoma, etc.

IT 358732-63-5P 358732-64-6P 358732-65-7P
358732-66-8P 358732-67-9P 358732-68-0P
358732-69-1P 358732-70-4P 358732-71-5P
358732-72-6P, 2-0xo-3-(4-0xo-2,4,6,7-tetrahydropyrano[3,4-c]pyrrol-1-ylmethylene)-2,3-dihydro-1H-indole-5-sulfonic acid amide
358732-73-7P 358732-74-8P 358732-75-9P
358732-76-0P, N-[2-0xo-3-(4-0xo-2,4,6,7-tetrahydropyrano[3,4-c]pyrrol-1-ylmethylene)-2,3-dihydro-1H-indol-6-yl]acetamide
358732-77-1P 358732-78-2P 358732-79-3P,
2-0xo-3-(4-0xo-2,4,6,7-tetrahydropyrano[3,4-c]pyrrol-1-ylmethylene)-

2-Oxo-3-(4-oxo-2,4,6,7-tetrahydropyrano[3,4-c]pyrrol-1-ylmethylene)-2,3-dihydro-1H-indole-5-carboxylic acid **358732-80-6P**,

2-0xo-3-(4-oxo-2,4,6,7-tetrahydropyrano[3,4-c]pyrrol-1-ylmethylene)-2,3-14-0xo-2,4,6,7-tetrahydropyrano[3,4-c]pyrrol-1-ylmethylene)-2,4-14-0xo-

dihydro-1H-indole-6-carboxylic acid 358732-81-7P

358732-82-8P 358732-83-9P 358732-84-0P 358732-85-1P 358732-86-2P 358732-87-3P

358732-88-4P 358732-90-8P 358732-92-0P

358732-94-2P 358732-96-4P 358732-98-6P

358732-99-7P 358733-00-3P 358733-01-4P,

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3-[2-0xo-3-(4-oxo-2,4,6,7-tetrahydropyrano[3,4-c]pyrrol-1-ylmethylene)-2,3-
     dihydro-1H-indol-5-yl]benzoic acid 358733-03-6P,
     3-[2-0xo-3-(4-0xo-2,4,6,7-tetrahydropyrano[3,4-c]pyrrol-1-ylmethylene)-2,3-
     dihydro-1H-indol-6-yl]benzoic acid 358733-05-8P
     358733-06-9P 358733-07-0P 358733-08-1P
     358733-09-2P 358733-10-5P 358733-11-6P
     358733-12-7P 358733-13-8P 358733-14-9P
     358733-15-0P 358733-16-1P 358733-17-2P
     358733-18-3P 358733-19-4P 358733-20-7P
     358733-21-8P 358733-23-0P 358733-24-1P
     358733-25-2P 358733-26-3P 358733-27-4P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (drug; synthesis of Pyrolyllactone-indolinone derivs. as kinase
        inhibitors)
IT
     150977-45-0, Flk-1 receptor tyrosine kinase
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (synthesis of Pyrolyllactone-indolinone derivs. as kinase inhibitors)
L18 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2001 ACS
                         2001:617993 HCAPLUS
ACCESSION NUMBER:
                         135:195497
DOCUMENT NUMBER:
TITLE:
                         Preparation of pyrrole substituted 2-indolinone
                         protein kinase inhibitors for treatment of cancer
                         Tang, Peng Cho; Miller, Todd; Li, Xiaoyuan; Sun, Li;
INVENTOR(S):
                         Wei, Chung Chen; Shirazian, Shahrzad; Liang, Congxin;
                         Vojkovsky, Tomas; Nematalla, Asaad S.
                         Sugen, Inc., USA
PATENT ASSIGNEE(S):
SOURCE:
                         PCT Int. Appl., 225 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                      KIND
                            DATE
                                           APPLICATION NO.
                                                            DATE
                      ____
                                           _____
                                          WO 2001-US4813 20010215
                     A2
                            20010823
            AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
             CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
             HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,
             LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
             SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
             YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
        RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
             DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
             BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
                                        US 2000-182710
                                                         P 20000215
PRIORITY APPLN. INFO.:
                                        US 2000-216422
                                                         P 20000706
                                        US 2000-243532
                                                         P 20001027
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MARPAT 135:195497

OTHER SOURCE(S):

GT

Ι

$$R^{2}$$
 R^{1}
 R^{1}
 R^{1}
 R^{1}
 R^{2}
 R^{3}
 R^{4}
 R^{1}
 R^{2}
 R^{3}
 R^{4}
 R^{5}

The title compds. (I) [wherein R1 = H, halo, (cyclo)alkyl, (hetero)aryl, AΒ heteroalicyclic, OH, alkoxy, acyl, (un) substituted amino or carbamoyl, etc.; R2 = H, halo, alkyl, trihalomethyl, OH, alkoxy, CN, (hetero)aryl, (un) substituted amino, acyl(amino), or sulfamoyl, etc.; R3 = H, halo, alkyl, trihalomethyl, OH, alkoxy, (hetero)aryl, (un)substituted acyl, (acyl)amino, sulfamoyl, or alkylsulfonyl, etc.; R4 = H, halo, alkyl, OH, alkoxy, or (un) substituted amino; R5 and R6 = independently H, alkyl, or acyl; R7 = H, alkyl, (hetero)aryl, or acyl; and their pharmaceutically .acceptable salts] were prepd. as protein kinase modulators for the treatment of cellular disorders such as cancer. For example, 5-fluoro-1,3-dihydroindol-2-one was condensed with 5-formyl-2,4-dimethyl-1H-pyrrole-3-carboxylic acid (2-diethylaminoethyl)amide to give II (55%). II exhibited comparable activity against Flk-1 and PDGFR.beta. and inhibited PDGF-dependent receptor phosphorylation in cells with an IC50 value of approx. 0.03 .mu.M. In efficacy expts. against various cancers in mice, II was well tolerated at 80 mg/kg/day, even when dosed continuously for more than 100 days.

TI

IT 356068-93-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (intermediate; prepn. of pyrrole substituted 2-indolinone protein kinase inhibitors by condensation of dihydroindolones with formylpyrroles for treatment of cancer and other diseases)

326914-13-0P

ΙT

RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of pyrrole substituted 2-indolinone protein kinase

inhibitors by condensation of dihydroindolones with

formylpyrroles for treatment of cancer and other diseases)

IT 280748-39-2P 280748-40-5P 326914-09-4P

326914-10-7P 326914-17-4P 326914-19-6P

342641-16-1P 342641-17-2P 342641-18-3P

342641-19-4P 342641-20-7P 342641-21-8P

342641-22-9P 342641-23-0P 342641-24-1P

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342641-25-2P 342641-26-3P 342641-27-4P
342641-28-5P 342641-29-6P 342641-30-9P
342641-31-0P 342641-32-1P 342641-33-2P
342641-35-4P 342641-36-5P 342641-37-6P
342641-38-7P 342641-39-8P 342641-40-1P
342641-41-2P 342641-42-3P 342641-43-4P
342641-44-5P 342641-45-6P 342641-46-7P
342641-47-8P 342641-48-9P 342641-49-0P
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356069-70-0P 356069-71-1P 356069-72-2P
356069-73-3P 356069-74-4P 356069-75-5P
356069-76-6P 356069-77-7P
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
   (prepn. of pyrrole substituted 2-indolinone protein kinase
```

inhibitors by condensation of dihydroindolones with formylpyrroles for treatment of cancer and other diseases)

342641-53-6 356069-06-2 356069-08-4 ΙT

356069-10-8 356069-14-2

RL: RCT (Reactant)

(reactant; prepn. of pyrrole substituted 2-indolinone protein kinase inhibitors by condensation of dihydroindolones with formylpyrroles for treatment of cancer and other diseases)

L18 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 2001:380529 HCAPLUS

DOCUMENT NUMBER:

134:366685

TITLE:

Preparation and use of 4-(benzyloxy)phenylalkanoic acid plasminogen activator inhibitor antagonists

ADDITION NO

INVENTOR(S):

Madison, Edwin L.; Brunck, Terence K.; Semple, Joseph Edward; Lim-Wilby, Marguerita; Pryor, Kent E.; Lewis, Ronald D., II; Duncan, David F.; Lawrence, C. Maxwell Corvas International, Inc., USA

PATENT ASSIGNEE(S):

PCT Int. Appl., 261 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

DAME

KEND

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION: DAMENIE NO

PAT	PATENT NO.				KIND DA				APPLICATION NO.				J.	DATE				
WO	2001036351			 A:	2	2001	0010525			WO 2000-US3182				24 20001117				
	W:	ΑE,	AG,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,	CR,	
		CU,	CZ,	DE,	DK,	DM,	DZ,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	
		ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	ΚP,	KR,	ΚZ,	LC,	LK,	LR,	LS,	LT,	LU,	
•		LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NO,	ΝŹ,	PL,	PΤ,	RO,	RU,	SD,	
		SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	ΤZ,	UA,	UG,	US,	UZ,	VN,	YU,	
		ZA,	ZW,	AM,	ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM						
	RW:	GH,	GM,	ΚE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZW,	ΑT,	BE,	CH,	CY,	
		DE,	DK,	ES,	FI,	FR,	GB,	GR,	ΙE,	IT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	
		ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG			
PRIORITY	.:	US 1999-444172 A2								A2								
US 2000-185564											64	Р						
	US 2000-580535												A2	2000	0526			

OTHER SOURCE(S):

MARPAT 134:366685

GI

$$(R^1)_m$$

$$(R^2)_n$$

$$(R^3)_p$$

Title compds. (I) [wherein R1 = independently (pseudo)halo, (halo)alkoxy, AΒ aryl, or (halo)alkyl; m = 0-4; q = 0-6; when n = 1-5 and p = 0, R2 and R3 = independently NO2, CN, (hetero)arylcarbonyl, haloalkylthio, (pseudo) halo, (cyclo) alkyl, (hetero) aryl, (cyclo) alkoxy, (hetero) aryloxy, haloalkyl, or haloalkoxy; or when n and p = 1, R2 and R3 together with the C atoms to which they are attached form a (hetero)arom. ring or (hetero)cyclic ring] and pharmaceutical compns. were prepd. as plasminogen activator inhibitor (PAI) antagonists for treatment of thrombotic disorders, unstable angina, cancer, and hemostatic disorders. In particular, methods of antagonizing PAI with substituted and unsubstituted aryl and heteroaryl ethers and thioethers, benzils, benzyl ethers, benzoate esters, sulfones, and benzophenones are provided. For example, a suspension of 3,5-diiodo-4-hydroxybenzoic acid, 3-bromobenzyl bromide, and Cs2CO3 in DMF was stirred for 15 h at room temp. to give 4-(3-bromobenzyloxy)-3,5-diiodobenzoic acid 3-bromobenzyl ester (84%). The IC50 for PAI antagonist activity for each of the disclosed compds. was measured, and most exhibited IC50 < 100 .mu.M.

IT 340314-10-5P, 3-(4-Hydroxy-3,5-diiodobenzylidene)-1,3-dihydroindol-2-one

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. and use of 4-(benzyloxy)phenylalkanoic acid plasminogen activator inhibitor antagonists for treatment of thrombotic disorders, unstable angina, cancer, and hemostatic disorders)

L18 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2001 ACS ACCESSION NUMBER: 2001:240686 HCAPLUS

DOCUMENT NUMBER: 135:2309

DOCUMENT NUMBER: 155:2509

TITLE: Inhibition of vascular endothelial growth factor

receptor signaling leads to reversal of tumor

resistance to radiotherapy

AUTHOR(S): Geng, Ling; Donnelly, Edwin; McMahon, Gerald; Lin, P.

Charles; Sierra-Rivera, Elaine; Oshinka, Halina;

Hallahan, Dennis E.

CORPORATE SOURCE: Departments of Radiation Oncology, Vanderbilt

University School of Medicine, Vanderbilt University,

Nashville, TN, 37232, USA

SOURCE: Cancer Res. (2001), 61(6), 2413-2419

CODEN: CNREA8; ISSN: 0008-5472

PUBLISHER: American Association for Cancer Research

DOCUMENT TYPE: Journal LANGUAGE: English

Certain refractory neoplasms, such as glioblastoma multiforme (GBM) and AB melanoma, demonstrate a resistant tumor phenotype in vivo. We obsd. that these refractory tumor models (GBM and melanoma) contain blood vessels that are relatively resistant to radiotherapy. To det. whether the vascular endothelial growth factor receptor-2 (Flk-1/KDR) may be a therapeutic target to improve the effects of radiotherapy, we used the sol. extracellular component of Flk-1 (ExFlk), which blocks vascular endothelial growth factor binding to Flk-1 receptor expressed on the tumor endothelium. Both sFlk-1 and the Flk -1-specific inhibitor SU5416 eliminated the resistance phenotype in GBM and melanoma microvasculature as detd. by both the vascular window and Doppler blood flow methods. Human microendothelial cells and human umbilical vein endothelial cells showed minimal radiation-induced The Flk-1 antagonists sFlk-1 and SU5416 reverted these cell models to apoptosis-prone phenotype. Flk-1 antagonists also reverted GBM and melanoma tumor models to radiation-sensitive phenotype after treatment with 3 Gy. These findings demonstrate that the tumor microenvironment including the survival of tumor-assocd. endothelial cells contributes to tumor blood vessel resistance to therapy.

204005-46-9, SU 5416

OTHER SOURCE(S):

GI

IT

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RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (tumor vascularization inhibitor; inhibition of
        VEGF receptor signaling enhances radiation-induced response in tumor
        blood vessels)
REFERENCE COUNT:
REFERENCE(S):
                         (2) Advani, S; Gene Ther 1998, V5, P160 HCAPLUS
                         (9) Fong, T; Cancer Res 1999, V59, P99 HCAPLUS
                         (10) Gerber, H; J Biol Chem 1998, V273, P13313 HCAPLUS
                          (11) Goldman, C; Proc Natl Acad Sci USA 1998, V95,
                             P8795 HCAPLUS
                         (12) Gorski, D; Cancer Res 1999, V59, P3374 HCAPLUS
                         ALL CITATIONS AVAILABLE IN THE RE FORMAT
L18 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2001 ACS
                         2000:688215 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         133:252306
                         Preparation of indolinones as protein kinase
TITLE:
                         inhibitors.
INVENTOR(S):
                         Tang, Peng Cho; Sun, Li; Mcmahon, Gerald; Miller, Todd
                         Anthony; Shirazian, Shahrzad; Wei, Chung Chen; Harris,
                         G. Davis; Xiaoyuan, Li; Liang, Congxin
                         Sugen, Inc., USA
PATENT ASSIGNEE(S):
                         PCT Int. Appl., 245 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
                                           APPLICATION NO.
                                                           DATE
     PATENT NO.
                      KIND
                            DATE
                                         WO 2000-US7704
    WO 2000056709
                      A1
                            20000928
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             ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
             LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
             SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA,
             ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                        US 1999-125945
                                                          P 19990324
                                        US 1999-127863
                                                          P 19990405
                                        US 1999-131192
                                                          P 19990426
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MARPAT 133:252306

US 1999-132243

P 19990503

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LR13 R3
                                   Ι
     Title compds., e.g. [I; m, n = 0, 1; Q = (JR11)m; Q1 = (DR6)n; when n = 1,
AB
     then A, B, D, E, F = C, N; .ltoreq.3 of A, B, D, E, F = N; when m = 1, then G, H, J, K, L = C, N; .gtoreq.1 and .ltoreq.3 of G, H, J, K, L = N; when n = 0, then A = C, N, B, F = C, N, NH, O, S; E = C, N, O, S; when m = \frac{1}{2}
     O, then G = C, N, H, K, I = C, N, NH, O, S; R1-R13 = H, alkyl,
     trihaloalkyl, cycloalkyl, alkenyl, alkynyl, aryl, heteroaryl, OH, alkoxy,
     SH, alkylthiol, aryloxy, amino, etc.; R4R5 or R5R6 or R6R7 or R7R8 = atoms
     to form a 5-6 membered (hetero)aryl ring; with addnl. provisos], were
     prepd. Thus, 6-pyridin-3-yl-1,3-dihydroindol-2-one (prepn. given),
     4-methoxy-3-thien-2-ylbenzaldehyde, and piperidine were refluxed overnight
     in EtOH to give 15% 3-(4-methoxy-3-thien-2-ylbenzylidene)-6-pyridin-3-yl-
     1,3-dihydroindol-2-one. Tested title compds. inhibited HER2 kinase with
     IC50 = 16.4 .mu.M to .gtoreq.100 .mu.M.
     295798-91-3P 295798-95-7P
ΙT
     RL: BAC (Biological activity or effector, except adverse); RCT (Reactant);
     SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological
     study); PREP (Preparation); USES (Uses)
         (prepn. of indolinones as protein kinase inhibitors)
     251356-74-8P 295798-93-5P 295798-97-9P
ΙT
     295798-99-1P 295799-27-8P 295799-29-0P
     295799-31-4P 295799-33-6P 295799-35-8P
     295799-37-0P 295799-39-2P 295799-41-6P
     295799-43-8P 295799-47-2P 295799-51-8P
     295799-97-2P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
         (prepn. of indolinones as protein kinase inhibitors)
     258828-94-3 258829-04-8 258829-17-3
IT
     258829-24-2 295800-19-0 295800-20-3
     295800-21-4 295800-22-5 295800-23-6
     295800-24-7
     RL: RCT (Reactant)
         (prepn. of indolinones as protein kinase inhibitors)
     251356-61-3P 251356-63-5P 251356-65-7P
TΤ
     251356-66-8P 251356-67-9P 251356-68-0P
     258829-01-5P 295800-04-3P 295800-06-5P
     295800-07-6P 295800-08-7P 295800-09-8P
     295800-25-8P
```

(1) Andreani; DATABASE CHEMABS HCAPLUS

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)

(prepn. of indolinones as protein kinase inhibitors)

31

REFERENCE COUNT:

REFERENCE(S):

(3) Decodts; DATABASE CHEMABS HCAPLUS.

HCAPLUS

(2) Andreani; EUR J MED CHEM 1990, V25(2), P187

```
(4) Decodts; EUR J MED CHEM - CHIM THER 1983, V18(2),
                             P107 HCAPLUS
                         (5) Erba Carlo Spa; WO 9113055 A 1991 HCAPLUS
                         ALL CITATIONS AVAILABLE IN THE RE FORMAT
L18 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2001 ACS
ACCESSION NUMBER:
                         2000:622463 HCAPLUS
                         133:217719
DOCUMENT NUMBER:
                         3-(Cyclohexanoheteroarylidenyl)-2-indolinone protein
TITLE:
                         tyrosine kinase inhibitors, and their therapeutic use
INVENTOR(S):
                         Tang, Peng Cho; Sun, Li; McMahon, Gerald; Blake,
                         Robert A.
PATENT ASSIGNEE (S):
                         Sugen, Inc., USA
                         U.S., 61 pp., Cont. -in-part of U.S. Ser. No. 99,842.
SOURCE:
                         CODEN: USXXAM
DOCUMENT TYPE:
                         Patent
                         English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                      KIND DATE
                                           APPLICATION NO. DATE
                      ____
                                           US 1998-190970
                            20000905
                                                            19981112
     US 6114371
                       Α
                                           US 1998-99842
                                                            19980619
     US 6130238
                      Α
                            20001010
                                        US 1997-50977 P 19970620
PRIORITY APPLN. INFO.:
                                                        P 19970919
                                        US 1997-59384
                                                         A2 19980619
                                        US 1998-99842
                                        US 1997-59544
                                                        P 19970919
                         CASREACT 133:217719; MARPAT 133:217719
OTHER SOURCE(S):
     3-(Cyclohexano-heteroarylidenyl)-2-indolinone compds., and physiol.
AΒ
     acceptable salts and prodrugs thereof, are disclosed which are expected to
     modulate the activity of protein tyrosine kinases and therefore to be
     useful in the prevention and treatment of protein tyrosine kinase-related
     cellular disorders (cancer, arthritis, restenosis, etc.).
     215543-90-1 215543-91-2 245035-88-5
IT
     245035-93-2 245035-96-5 245036-00-4
     245036-07-1 245036-08-2 245036-21-9
     245036-22-0 290821-14-6 290821-15-7
     290821-16-8 290821-17-9 290821-18-0
     290821-19-1 290821-20-4
     RL: BAC (Biological activity or effector, except adverse); THU
     (Therapeutic use); BIOL (Biological study); USES (Uses)
        (cyclohexanoheteroarylidenyl indolinone protein tyrosine kinase
        inhibitors, and therapeutic use)
     150977-45-0, Flk-1 receptor tyrosine kinase
IT
     RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
        (cyclohexanoheteroarylidenyl indolinone protein tyrosine kinase
        inhibitors, and therapeutic use)
REFERENCE COUNT:
                         38
REFERENCE(S):
                         (1) Akbasak; J Neurol Sci 1992, V111, P119 HCAPLUS
                         (2) Andreani; Eur J Med Chem 1997, V32, P919 HCAPLUS
                         (3) Anon; WO 9115495-1991 HCAPLUS
                         (4) Anon; WO 9220642 1992 HCAPLUS
                         (5) Anon; WO 9221660 1992 HCAPLUS
                         ALL CITATIONS AVAILABLE IN THE RE FORMAT
```

L18 ANSWER 7 OF 17 HCAPLUS COPYRIGHT 2001 ACS

2000:509389 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

134:216785

TITLE:

New anilinophthalazines as potent and orally well absorbed inhibitors of the VEGF receptor tyrosine kinases useful as antagonists of tumor-driven angiogenesis. [Erratum to document cited in

CA133:99079]

AUTHOR(S):

Bold, Guido; Altmann, Karl-Heinz; Frei, Joerg; Lang, Marc; Manley, Paul W.; Traxler, Peter; Wietfeld, Bernhard; Brueggen, Josef; Buchdunger, Elisabeth; Cozens, Robert; Ferrari, Stefano; Furet, Pascal; Hofmann, Francesco; Martiny-Baron, Georg; Mestan, Juergen; Roesel, Johannes; Sills, Matthew; Stover, David; Acemoglu, Figan; Boss, Eugen; Emmenegger, Rene; Laesser, Laurent; Masso, Elvira; Roth, Rosemarie;

Schlachter, Christian; Vetterli, Werner; Wyss,

Dominique; Wood, Jeanette M.

CORPORATE SOURCE:

Oncology Research and Process Research, NOVARTIS

Pharma AG, Basel, CH-4002, Switz. J. Med. Chem. (2000), 43(16), 3200

CODEN: JMCMAR; ISSN: 0022-2623

American Chemical Society PUBLISHER:

DOCUMENT TYPE:

Journal

LANGUAGE:

SOURCE:

English

On page 2316, in Table 3, the unit for cmax; the concn. should be given as · AB [.mu.M]. The correct version of Table 3 is given.

204005-46-9, SU 5416

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(prepn. of anilinophthalazines as inhibitors of VEGF receptor tyrosine kinase (Erratum))

L18 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

2000:500184 HCAPLUS

DOCUMENT NUMBER:

133:234344

TITLE:

DoMCoSAR: A Novel Approach for Establishing the

Docking Mode That Is Consistent with the

Structure-Activity Relationship. Application to HIV-1 Protease Inhibitors and VEGF Receptor Tyrosine Kinase

Inhibitors

AUTHOR(S):

Vieth, Michal; Cummins, David J.

CORPORATE SOURCE:

Lilly Research Laboratories, Eli Lilly and Company,

Indianapolis, IN, 46285, USA

SOURCE:

J. Med. Chem. (2000), 43(16), 3020-3032

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER:

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

DoMCoSAR is a novel approach for statistically detg. the docking mode that is consistent with a structure-activity relationship. The approach establishes the binding mode for the compds. in a chem. series with the assumption that all mols. exhibit the same binding mode. It involves three stages. In the first stage all mols. that belong to a given chem. series are docked to the active site of the protein target. The only bias used in the docking at this stage involves the location of the protein binding site. Coordinates of the common substructure (CS) that results from the unbiased docking are then clustered to establish the major

substructure docking modes. In the second stage all mols. are docked to the major docking modes (MDMs) with constraints based on the common substructure. The third stage generates, for the major docking modes, interaction-based descriptors that include electrostatic, VDW, strain, and solvation contributions. The problem of docking mode evaluation is now reduced to the question of which descriptor set is more predictive. To establish a quant. comparison of the descriptor sets assocd. with the major docking modes, we use 50 instances of random 4-fold cross-validation. For each 4-fold cross-validation the predictive squared correlation coeff. (R2) is computed. T-Tests are applied to establish significance of the differences in mean R for one docking mode vs. another. We test the methodol. on two test cases: HIV-1 protease inhibitors (Holloway et al. J. Med. Chem. 1995, 38, 305-317) and vascular endothelial growth factor (VEGF) receptor tyrosine kinase oxoindoles (Sun et al. J. Med. Chem. 1998, 41, 2588-2603). For both test cases there is statistically significant preference for the binding mode consistent with the x-ray structure. The appeal of this methodol. is that researchers gain the objectivity of statistical justification for the selected docking mode. The methodol. is relatively insensitive to subtle variations of the protein structure that include, but are not limited to, side chain and small backbone rearrangement during binding. In addn., predictive models that result from the approach can be used to further optimize chem. series.

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ΙT
    5812-07-7 15966-93-5 40526-64-5
    55160-02-6 64259-01-4 64259-05-8
    76086-99-2 91822-51-4 108402-27-3
    186610-88-8 186610-89-9 186610-90-2
    186610-94-6 186610-96-8 186611-10-9
    186611-25-6 186611-27-8 186611-28-9
    186611-29-0 186611-37-0 186611-38-1
    186611-40-5 186611-45-0 186611-47-2
    186611-48-3 186611-53-0 186611-55-2
    186611-65-4 204005-46-9 204005-54-9
    293302-08-6 293302-09-7 293302-10-0
    293302-11-1 293302-12-2 293302-13-3
    293302-14-4 293302-15-5 293302-16-6
    293302-17-7 293302-18-8 293302-19-9
    293302-20-2 293302-22-4 293302-23-5
    293302-24-6 293302-25-7 293302-26-8
    293302-27-9 293302-28-0
    RL: BPR (Biological process); PRP (Properties); THU (Therapeutic use);
    BIOL (Biological study); PROC (Process); USES (Uses)
        (VEGF kinase-inhibitor; DoMCoSAR - novel approach for
       establishing docking mode that is consistent with structure-activity
       relationship with application to HIV-1 protease inhibitors
       and VEGF receptor tyrosine kinase inhibitors)
    150977-45-0, Flk-1/KDR VEGF receptor tyrosine kinase
```

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(inhibitors; DoMCoSAR - novel approach for establishing docking mode that is consistent with structure-activity relationship with application to HIV-1 protease inhibitors and VEGF receptor tyrosine kinase inhibitors)

REFERENCE COUNT:

REFERENCE(S):

- (1) Altschul, S; Nucleic Acid Res 1997, V25, P3389 HCAPLUS
- (3) Brooks, B; J Comput Chem 1983, V4, P187 HCAPLUS
- (5) Brown, R; J Chem Inf Comput Sci 1997, V37, P1

HCAPLUS

(7) Charifson, P; J Med Chem 1999, V42, P5100 HCAPLUS (10) Gallop, M; J Med Chem 1994, V37, P1233 HCAPLUS ALL CITATIONS AVAILABLE IN THE RE FORMAT

L18 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

2000:359936 HCAPLUS

DOCUMENT NUMBER:

133:99079

TITLE:

New Anilinophthalazines as Potent and Orally Well Absorbed Inhibitors of the VEGF Receptor Tyrosine Kinases Useful as Antagonists of Tumor-Driven

Angiogenesis

AUTHOR(S):

Bold, Guido; Altmann, Karl-Heinz; Frei, Joerg; Lang, Marc; Manley, Paul W.; Traxler, Peter; Wietfeld, Bernhard; Brueggen, Josef; Buchdunger, Elisabeth; Cozens, Robert; Ferrari, Stefano; Furet, Pascal; Hofmann, Francesco; Martiny-Baron, Georg; Mestan, Juergen; Roesel, Johannes; Sills, Matthew; Stover, David; Acemoglu, Figan; Boss, Eugen; Emmenegger, Rene; Laesser, Laurent; Masso, Elvira; Roth, Rosemarie; Schlachter, Christian; Vetterli, Werner; Wyss,

Dominique; Wood, Jeanette M.

CORPORATE SOURCE:

Oncology Research and Process Research, NOVARTIS

Pharma AG, Basel, CH-4002, Switz.

SOURCE:

PUBLISHER:

J. Med. Chem. (2000), 43(12), 2310-2323 CODEN: JMCMAR; ISSN: 0022-2623

American Chemical Society

DOCUMENT TYPE:

Journal

LANGUAGE:

English

The sprouting of new blood vessels, or angiogenesis, is AB necessary for any solid tumor to grow large enough to cause life-threatening disease. Vascular endothelial growth factor (VEGF) is one of the key promoters of tumor induced angiogenesis. VEGF receptors, the tyrosine kinases Flt-1 and KDR, are expressed on vascular endothelial cells and initiate angiogenesis upon activation by VEGF. 1-Anilino-(4-pyridylmethyl)-phthalazines, such as CGP 79787D (or PTK787 / ZK222584), reversibly inhibit Flt-1 and KDR with IC50 values < 0.1 .mu.M. CGP 79787D also blocks the VEGF-induced receptor autophosphorylation in CHO cells ectopically expressing the KDR receptor (ED50 = 34 nM). Modification of the 1-anilino moiety afforded derivs. with higher selectivity for the VEGF receptor tyrosine kinases Flt-1 and KDR compared to the related receptor tyrosine kinases PDGF-R and c-Kit. Since these 1-anilino-(4-pyridylmethyl)phthalazines are orally well absorbed, these compds. qualify for further profiling and as candidates for clin. evaluation.

204005-46-9, SU 5416 ΙT

> RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)

(prepn. of anilinophthalazines as inhibitors of VEGF receptor tyrosine kinase)

REFERENCE COUNT:

REFERENCE(S):

- (1) Andersen, L; Acta Chem Scand, Ser B 1988, VB42, P492 HCAPLUS
- (2) Augustin, H; Trends Pharmacol Sci 1998, V19, P216 HCAPLUS
- (3) Bergers, G; Science 1999, V284, P808 HCAPLUS
- (4) Bold, G; WO 9835958 A1 1998 HCAPLUS
- (5) Breier, G; Trends Cell Biol 1996, V6, P454 HCAPLUS

ALL CITATIONS AVAILABLE IN THE RE FORMAT

HCAPLUS COPYRIGHT 2001 ACS L18 ANSWER 10 OF 17 1999:757553 HCAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 132:137242

TITLE: Design, Synthesis, and Evaluations of Substituted

3-[(3- or 4-Carboxyethylpyrrol-2-

yl)methylidenyl]indolin-2-ones as Inhibitors of VEGF,

FGF, and PDGF Receptor Tyrosine Kinases

Sun, Li; Tran, Ngoc; Liang, Congxin; Tang, Flora; AUTHOR(S):

Rice, Audie; Schreck, Randall; Waltz, Kara; Shawver,

Laura K.; McMahon, Gerald; Tang, Cho

SUGEN Inc., South San Francisco, CA, 94080-4811, USA CORPORATE SOURCE:

J. Med. Chem. (1999), 42(25), 5120-5130 SOURCE:

CODEN: JMCMAR; ISSN: 0022-2623

American Chemical Society PUBLISHER:

DOCUMENT TYPE: Journal LANGUAGE: English

Receptor tyrosine kinases (RTKs) were implicated as therapeutic targets for the treatment of human diseases including cancers, inflammatory diseases, cardiovascular diseases including arterial restenosis, and fibrotic diseases of the lung, liver, and kidney. Three classes of 3-substituted 2-indolinones contg. propanoic acid functionality attached to the pyrrole ring at the C-3 position of the core were identified as catalytic inhibitors of the vascular endothelial growth factor (VEGF), fibroblast growth factor (FGF), and platelet-derived growth factor (PDGF) RTKs. Some of the compds. were found to inhibit the tyrosine kinase activity assocd. with isolated vascular endothelial growth factor receptor 2 (VEGF-R2) [fetal liver tyrosine kinase 1 (Flk-1)/kinase insert domain-contg. receptor (KDR)], fibroblast growth factor receptor (FGF-R), and platelet-derived growth factor receptor (PDGF-R) tyrosine kinase with IC50 values at nanomolar level. Thus, SU 5402 [5-[(1,2-dihydro-2-oxo-3Hindol-3-ylidene)methyl]-4-methyl-1H-Pyrrole-3-propanoic acid] showed inhibition against VEGF-R2 (Flk-1/KDR) and FGF-R1 tyrosine kinase activity with IC50 values of 20 and 30 nM, resp., while 5-[(1,2-dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1Hpyrrole-3-propanoic acid inhibited the PDGF-R tyrosine kinase activity with IC50 value of 10 nM. Structural models and structure-activity relationship anal. of these compds. for the target receptors are The cellular activities of these compds. were profiled using cellular proliferation assays as measured by bromodeoxyuridine (BrdU) incorporation. Specific and potent inhibition of cell growth was obsd. for some of these compds. These data provide evidence that these compds. can be used to inhibit the function of these target receptors.

256657-46-2 256657-47-3 256657-51-9 IT

> RL: BAC (Biological activity or effector, except adverse); BIOL (Biological study)

(prepn. and evaluation of [(dihydrooxoindolylidene)methyl]pyrrolepropan oic acid as tyrosine kinase inhibitors)

186611-14-3P, 5-[(1,2-Dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4methyl-1H-Pyrrole-3-propanoic acid 245036-27-5P, 5-[(1,2-Dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-Pyrrole-3propanoic acid 251356-17-9P, 5-[(1,2-Dihydro-6-methoxy-2-oxo-3Hindol-3-ylidene)methyl]-4-methyl-1H-Pyrrole-3-propanoic acid 251356-26-0P 251356-27-1P 251356-32-8P, 5-[(5-Bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-Pyrrole-3-propanoic acid 251356-38-4P, 5-[(1,2-Dihydro-6-methoxy-

2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-1H-Pyrrole-3-propanoic acid 251356-40-8P, 5-[(1,2-Dihydro-6-(3-methoxyphenyl)-2-oxo-3H-indol-3-

```
ylidene)methyl]-2,4-dimethyl-1H-Pyrrole-3-propanoic acid
     251356-42-0P, 5-[[1,2-Dihydro-6-(3-methoxyphenyl)-2-oxo-3H-indol-3-
     ylidene]methyl]-4-methyl-1H-Pyrrole-3-propanoic acid 251356-45-3P
     , 5-[(1,2-Dihydro-2-oxo-6-phenyl-3H-indol-3-ylidene)methyl]-2,4-dimethyl-
     1H-pyrrole-3-propanoic acid 251356-46-4P, 5-[[1,2-Dihydro-2-oxo-
     6-phenyl-3H-indol-3-ylidene]methyl]-4-methyl-1H-Pyrrole-3-propanoic acid
     251356-47-5P, 5-[[1,2-Dihydro-6-(4-methoxyphenyl)-2-oxo-3H-indol-3-
     ylidene]methyl]-4-methyl-1H-Pyrrole-3-propanoic acid 251356-48-6P
     , 5-[(1,2-Dihydro-6-(4-methoxyphenyl)-2-oxo-3H-indol-3-ylidene)methyl]-2,4-
     dimethyl-1H-Pyrrole-3-propanoic acid 251356-49-7P,
     5-[[1,2-Dihydro-6-(2-methoxyphenyl)-2-oxo-3H-indol-3-ylidene]methyl]-4-
     methyl-1H-Pyrrole-3-propanoic acid 251356-50-0P,
     5-[(1,2-Dihydro-6-(2-methoxyphenyl)-2-oxo-3H-indol-3-ylidene)methyl]-2,4-
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     256657-64-4P 256657-65-5P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); BIOL (Biological study); PREP (Preparation)
        (prepn. and evaluation of [(dihydrooxoindolylidene)methyl]pyrrolepropan
        oic acid as tyrosine kinase inhibitors)
     204005-46-9, SU 5416 215543-92-3
ΙT
     RL: BSU (Biological study, unclassified); BIOL (Biological study)
        (prepn. and evaluation of [(dihydrooxoindolylidene)methyl]pyrrolepropan
        oic acid as tyrosine kinase inhibitors)
REFERENCE COUNT:
                         15
                         (1) Cantley, L; Cell 1991, V64, P281 HCAPLUS
REFERENCE(S):
                         (3) Hanks, S; Methods Enzymol 1991, V200, P38 HCAPLUS
                         (4) Kolibaba, K; Biochim Biophys Acta 1997, V1333,
                             PF217 HCAPLUS
                         (5) Merenmies, J; Cell Growth Differ 1997, V8, P3
                             HCAPLUS
                         (6) Mohammadi, M; EMBO J 1998, V17(20), P5896 HCAPLUS
                         ALL CITATIONS AVAILABLE IN THE RE FORMAT
L18 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2001 ACS
                         1999:166598 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         130:209599
                         Preparation of benzylidene-1, 3-dihydroindol-2-ones as
TITLE:
                         receptor tyrosine kinase inhibitors.
                         McNutt, Robert Walton, Jr.; Jung, David Kendall;
INVENTOR(S):
                         Harris, Philip Anthony; Hunter, Robert Neil, III;
                         Veal, James Marvin; Dickerson, Scott; Lackey, Karen
                         Elizabeth; Peel, Michael Robert
PATENT ASSIGNEE(S):
                         Glaxo Group Limited, UK
                         PCT Int. Appl., 144 pp.
SOURCE:
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
                         English
LANGUAGE:
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
     PATENT NO.
                      KIND
                            DATE
                                           APPLICATION NO.
                      ____
                            _____
                                           _____
                      A1
                            19990304
                                          WO 1998-EP4844 19980804
         W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE,
             DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG,
             KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
             NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT,
             UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
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FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG AU 9891584 Αl 19990316 AU 1998-91584 19980804 20000531 EP 1998-943832 19980804 EP 1003721 A1 AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, R: IE, FI US 6268391 20010731 US 2000-446586 20000407 В1 PRIORITY APPLN. INFO.: GB 1997-16557 Α 19970806 WO 1998-EP4844 W 19980804 OTHER SOURCE(S): MARPAT 130:209599

$$R^{2}$$
 R^{3}
 R^{4}
 R^{5}
 R^{8}
 R^{7}
 R^{7}

Title compds. [I; R1 = H; R1R2 = fused 5-10 membered aryl, heteroaryl, AΒ heterocyclyl; R2, R3 = H, HET, aryl, aliphatyl, cyano, NO2, halo, R10, OR10, SR10, SOR10, SO2R10, NR10R11, etc.; R4 = H, halo, NO2, cyano; R5 = H, (substituted) aliphatyl; R6, R7 = halo, cyano, NO2, CONR10R11, SO2NR10R11, NR10R11, OR11; R8 = OH, NHSO2R12, NHCOCF3; R10 = H, halo, (substituted) aliphatyl, aryl, HET; R11 = H, R10; R12 = H, (substituted) aliphatyl, HET; HET = benzofuryl, benzoxazolyl, dioxanyl, dithianyl, dithiazinyl, furyl, imidazolyl, indolyl, indazolyl, morpholinyl, tetrazolyl, pyrrolyl, quinolinyl, triazinyl, tetrahydrofuryl, etc.], were prepd. for treatment of tumor growth, preventing organ transplant rejection, healing chronic wounds, etc. (no data). Thus, 5-(2-methylthiazol-4-yl)-1,3-dihydroindol-2-one hydrochloride (prepn. qiven) was stirred with 3,5-dibromo-4-hydroxybenzaldehyde in AcOH/aq. HCl to give 64% 3-(3,5-dibromo-4-hydroxybenzylidene)-5-(2-methylthiazol-4-yl)-1,3-dihydroindol-2-one.

IT 220904-54-1P 220904-55-2P 220904-56-3P 220904-57-4P 220904-58-5P 220904-59-6P 220904-60-9P 220904-61-0P 220904-62-1P 220904-63-2P 220904-64-3P 220904-65-4P 220904-66-5P 220904-67-6P 220904-70-1P 220904-71-2P 220904-73-4P 220904-75-6P 220904-77-8P 220904-78-9P 220904-79-0P 220904-80-3P 220904-81-4P 220904-82-5P 220904-83-6P 220904-87-0P 220904-88-1P 220905-00-0P 220905-01-1P 220905-03-3P 220905-04-4P 220905-05-5P 220905-06-6P

Ι

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of benzylidene-1,3-dihydroindol-2-ones as receptor tyrosine kinase inhibitors.)

IT 220904-99-4

RL: RCT (Reactant)

(prepn. of benzylidene-1,3-dihydroindol-2-ones as receptor tyrosine kinase inhibitors.)

REFERENCE COUNT:

REFERENCE(S):

- (1) Merck & Co Inc; GB 2306108 A 1997 HCAPLUS
- (2) Sugen Inc; WO 9640116 A 1996 HCAPLUS
- (3) Sugen Inc; WO 9807695 A 1998 HCAPLUS
- (4) Tatho Pharmaceutical Co Ltd; WO 9725986 A 1997 **HCAPLUS**

L18 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1998:429042 HCAPLUS

DOCUMENT NUMBER:

129:117426

TITLE:

Synthesis and Biological Evaluations of 3-Substituted Indolin-2-ones: A Novel Class of Tyrosine Kinase Inhibitors That Exhibit Selectivity toward Particular

Receptor Tyrosine Kinases

AUTHOR(S):

SOURCE:

Sun, Li; Tran, Ngoc; Tang, Flora; App, Harald; Hirth,

Peter; McMahon, Gerald; Tang, Cho

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English 3-Substituted indolin-2-ones have been designed and synthesized as a novel class of tyrosine kinase inhibitors which exhibit selectivity toward different receptor tyrosine kinases (RTKs). These compds. have been evaluated for their relative inhibitory properties against a panel of RTKs in intact cells. By modifying the 3-substituted indolin-2-ones, we have identified compds. which showed selective inhibition of the ligand-dependent autophosphorylation of various RTKs at submicromolar levels in cells. Structure-activity anal. for these compds. and their relative potency and selectivity to inhibit particular RTKs has detd. that (1) 3-[(five-membered heteroaryl ring)methylidenyl]indolin-2-ones are highly specific against the VEGF (Flk-1) RTK activity, (2) 3-(substituted benzylidenyl)indolin-2-ones contg. bulky group(s) in the Ph ring at the C-3 position of indolin-2-ones showed high selectivity toward the EGF and Her-2 RTKs, and (3) the compd. contg. an extended side chain at the C-3 position of the indolin-2-one exhibited high potency and selectivity when tested against the PDGF and VEGF (Flk-1) RTKs. Recent published crystallog. data for two of these 3-substituted indolin-2-ones provides a rationale to suggest that these compds. may bind in the ATP binding pocket of RTKs. The structure-activity anal. supports the use of subsets of these compds. as specific chem. leads for the development of RTK-specific drugs with broad application for the treatment of human diseases.

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        (prepn. and evaluation of 3-substituted indolin-2-ones as
        inhibitors of selective growth factor receptors)
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                         Indolinone combinatorial libraries and related
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AΒ The invention relates to indolinone derivs. capable of modulating, regulating, and/or inhibiting protein kinase signal transduction. compds. are useful for the treatment of diseases related to unregulated protein kinase signal transduction, including cell proliferative diseases such as cancer, atherosclerosis, arthritis, and restenosis, and metabolic diseases such as diabetes. Inhibitors specific to the FLK protein kinase can be obtained by adding chem. substituents to the 3-[(indole-3-yl)methylene]-2-indolinone system, in particular at the 1' position of the indole ring. Indolinone compds. that specifically inhibit the FLK and platelet derived growth factor protein kinases can harbor a tetrahydroindole or cyclopentano[b]pyrrole moiety. compds. that are modified with substituents, particularly at the 5 position of the oxindole ring, can effectively activate protein kinases. This invention also features novel hydrosol. indolinone compds. that are tyrosine kinase inhibitors, and related products and methods. Approx. 1200 title compds., such as I, were prepd. by combinatorial condensation of certain (un)substituted indolinones with aldehydes at the 3-position. I gave complete inhibition of MET kinase at chimeric MET receptors in vitro.

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3-(2,4-Dihydroxy-3-methylbenzylidenyl)-5-(2-chloroethyl)-2-indolinone
203989-83-7P, 3-(Furan-2-ylmethylidenyl)-5-(2-chloroethyl)-2-
indolinone 203989-84-8P, 3-[(2-Nitrofuran-5-yl)methylidenyl]-5-
(2-chloroethyl)-2-indolinone 203989-85-9P, 3-(4-Ethoxy-3-
methoxybenzylidenyl)-5,7-dibromo-2-indolinone 203989-86-0P,
3-(3,4-Dihydroxybenzylidenyl)-5,7-dibromo-2-indolinone
203989-87-1P, 3-(2,4-Dimethoxybenzylidenyl)-5,7-dibromo-2-
indolinone 203989-88-2P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-
yl)methylidenyl]-5,7-dibromo-2-indolinone 203989-89-3P,
3-(2,4,6-Trimethoxybenzylidenyl)-5,7-dibromo-2-indolinone
203989-90-6P, 3-(4-Hydroxybenzylidenyl)-5,7-dibromo-2-indolinone
203989-91-7P, 3-[4-(Dimethylamino)benzylidenyl]-5,7-dibromo-2-
indolinone 203989-92-8P, 3-(2-Chloro-4-fluorobenzylidenyl)-5,7-
dibromo-2-indolinone 203989-93-9P, 3-(3-Nitrobenzylidenyl)-5,7-
dibromo-2-indolinone 203989-94-0P, 3-[4-Fluoro-2-
(\verb|trifluoromethy||) \verb|benzylideny||]-5, 7-dibromo-2-indolinone|
203989-95-1P, 3-(4-Ethoxy-3-methoxybenzylidenyl)-5-iodo-2-
indolinone 203989-96-2P, 3-(3,4-Dihydroxybenzylidenyl)-5-iodo-2-
indolinone 203989-97-3P, 3-(2,4-Dimethoxybenzylidenyl)-5-iodo-2-
indolinone 203989-98-4P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-
yl)methylidenyl]-5-iodo-2-indolinone 203989-99-5P,
3-(2,4,6-Trimethoxybenzylidenyl)-5-iodo-2-indolinone 203990-00-5P
  3-(4-Hydroxybenzylidenyl)-5-iodo-2-indolinone 203990-01-6P,
3-[4-(Dimethylamino)benzylidenyl]-5-iodo-2-indolinone 203990-02-7P
  3-(2-Chloro-4-fluorobenzylidenyl)-5-iodo-2-indolinone
203990-03-8P, 3-(3-Nitrobenzylidenyl)-5-iodo-2-indolinone
203990-04-9P, 3-[4-Fluoro-2-(trifluoromethyl)benzylidenyl]-5-iodo-
2-indolinone 203990-05-0P, 3-(4-Ethoxy-3-methoxybenzylidenyl)-5-
bromo-4-methyl-2-indolinone 203990-06-1P, 3-(3,4-
Dihydroxybenzylidenyl)-5-bromo-4-methyl-2-indolinone 203990-07-2P
  3-(2,4-Dimethoxybenzylidenyl)-5-bromo-4-methyl-2-indolinone
203990-08-3P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-
bromo-4-methyl-2-indolinone 203990-09-4P, 3-(2,4,6-
Trimethoxybenzylidenyl)-5-bromo-4-methyl-2-indolinone 203990-10-7P
  3-(4-Hydroxybenzylidenyl)-5-bromo-4-methyl-2-indolinone
203990-11-8P, 3-[4-(Dimethylamino)benzylidenyl]-5-bromo-4-methyl-2-
indolinone 203990-12-9P, 3-(2-Chloro-4-fluorobenzylidenyl)-5-
bromo-4-methyl-2-indolinone 203990-13-0P, 3-(3-
Nitrobenzylidenyl)-5-bromo-4-methyl-2-indolinone 203990-14-1P,
3-[4-Fluoro-2-(trifluoromethyl)benzylidenyl]-5-bromo-4-methyl-2-indolinone
203990-15-2P, 3-(4-Ethoxy-3-methoxybenzylidenyl)-5-
[(methylamino)sulfonyl]-2-indolinone 203990-16-3P,
3-(3,4-Dihydroxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
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203990-17-4P, 3-(2,4-Dimethoxybenzylidenyl)-5-
    [(methylamino)sulfonyl]-2-indolinone 203990-18-5P,
    3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-
    [(methylamino)sulfonyl]-2-indolinone 203990-19-6P,
    3-(2,4,6-Trimethoxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
    203990-20-9P, 3-(4-Hydroxybenzylidenyl)-5-[(methylamino)sulfonyl]-
    2-indolinone 203990-21-0P, 3-[4-(Dimethylamino)benzylidenyl]-5-
    [(methylamino)sulfonyl]-2-indolinone 203990-22-1P,
    3-(2-Chloro-4-fluorobenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
    203990-23-2P, 3-(3-Nitrobenzylidenyl)-5-[(methylamino)sulfonyl]-2-
    indolinone 203990-24-3P, 3-[4-Fluoro-2-
    (trifluoromethyl)benzylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
    203990-25-4P, 3-(4-Ethoxy-3-methoxybenzylidenyl)-5-[[[4-
    (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203990-26-5P
      3-(3,4-Dihydroxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfo
   nyl]-2-indolinone 203990-27-6P, 3-(2,4-Dimethoxybenzylidenyl)-5-
    [[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
   203990-28-7P, 3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-
    [[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
   203990-29-8P, 3-(2,4,6-Trimethoxybenzylidenyl)-5-[[[4-
    (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203990-30-1P
      3-(4-Hydroxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-
    2-indolinone 203990-31-2P, 3-[4-(Dimethylamino)benzylidenyl]-5-
    [[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
    203990-32-3P
3-(2-Chloro-4-fluorobenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfon
   yl]-2-indolinone 203990-33-4P, 3-(3-Nitrobenzylidenyl)-5-[[[4-
    (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203990-34-5P
    , 3-[4-Fluoro-2-(trifluoromethyl)benzylidenyl]-5-[[[4-
    (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203990-35-6P
      3-(4-Ethoxy-3-methoxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
    203990-36-7P, 3-(3,4-Dihydroxybenzylidenyl)-5-(morpholinosulfonyl)-
    2-indolinone 203990-37-8P, 3-(2,4-Dimethoxybenzylidenyl)-5-
    (morpholinosulfonyl) -2-indolinone 203990-38-9P,
    3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-(morpholinosulfonyl)-2-
    indolinone 203990-39-0P, 3-(2,4,6-Trimethoxybenzylidenyl)-5-
    (morpholinosulfonyl)-2-indolinone 203990-40-3P,
    3-(4-Hydroxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
    203990-41-4P, 3-[4-(Dimethylamino)benzylidenyl]-5-
    (morpholinosulfonyl)-2-indolinone 203990-42-5P,
    3-(2-Chloro-4-fluorobenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
   203990-43-6P, 3-(3-Nitrobenzylidenyl)-5-(morpholinosulfonyl)-2-
    indolinone 203990-44-7P, 3-[4-Fluoro-2-
    (trifluoromethyl)benzylidenyl]-5-(morpholinosulfonyl)-2-indolinone
   203990-45-8P, 3-(4-Ethoxy-3-methoxybenzylidenyl)-5-(2-chloroethyl)-
    2-indolinone 203990-46-9P, 3-(3,4-Dihydroxybenzylidenyl)-5-(2-
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    Dimethoxybenzylidenyl)-5-(2-chloroethyl)-2-indolinone 203990-48-1P
      3-[(2,4-Dimethyl-3-ethylpyrrol-5-yl)methylidenyl]-5-(2-chloroethyl)-2-
    indolinone 203990-49-2P, 3-(2,4,6-Trimethoxybenzylidenyl)-5-(2-
    chloroethyl)-2-indolinone 203990-50-5P, 3-(4-
   Hydroxybenzylidenyl)-5-(2-chloroethyl)-2-indolinone 203990-51-6P
     3-[4-(Dimethylamino)benzylidenyl]-5-(2-chloroethyl)-2-indolinone
   203990-52-7P, 3-(2-Chloro-4-fluorobenzylidenyl)-5-(2-chloroethyl)-
    2-indolinone 203990-53-8P, 3-(3-Nitrobenzylidenyl)-5-(2-
   chloroethyl)-2-indolinone 203990-54-9P, 3-[4-Fluoro-2-
    (trifluoromethyl)benzylidenyl]-5-(2-chloroethyl)-2-indolinone
    203990-55-0P, 3-(2,4,6-Trifluorobenzylidenyl)-5,7-dibromo-2-.
    indolinone 203990-56-1P, 3-(4-Hydroxy-2-methoxybenzylidenyl)-5,7-
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dibromo-2-indolinone 203990-57-2P, 3-(3,4-Dimethoxybenzylidenyl)-
     5,7-dibromo-2-indolinone 203990-58-3P, 3-(2-Hydroxybenzylidenyl)-5,7-dibromo-2-indolinone 203990-59-4P, 3-(Benzylidenyl)-5,7-
     dibromo-2-indolinone 203990-60-7P, 3-[[2-(Methylthio)thien-5-
     yl)methylidenyl]-5,7-dibromo-2-indolinone 203990-61-8P,
     3-(2,4-Dihydroxy-6-methylbenzylidenyl)-5,7-dibromo-2-indolinone
     203990-62-9P, 3-(3-Ethoxy-4-hydroxybenzylidenyl)-5,7-dibromo-2-
     indolinone 203990-63-0P, 3-(2-Hydroxy-5-methoxybenzylidenyl)-5,7-
     dibromo-2-indolinone 203990-64-1P, 3-[(Imidazol-2-
     yl)methylidenyl]-5,7-dibromo-2-indolinone 203990-65-2P,
     3-(2,4,6-Trifluorobenzylidenyl)-5-iodo-2-indolinone 203990-66-3P
       3-(4-Hydroxy-2-methoxybenzylidenyl)-5-iodo-2-indolinone
     203990-67-4P, 3-(3,4-Dimethoxybenzylidenyl)-5-iodo-2-indolinone
203990-68-5P, 3-(2-Hydroxybenzylidenyl)-5-iodo-2-indolinone
     203990-69-6P, 3-(Benzylidenyl)-5-iodo-2-indolinone
203990-70-9P, 3-[[2-(Methylthio)thien-5-yl)methylidenyl]-5-iodo-2-
     indolinone 203990-71-0P, 3-(2,4-Dihydroxy-6-methylbenzylidenyl)-
     5-iodo-2-indolinone 203990-72-1P, 3-(3-Ethoxy-4-
     hydroxybenzylidenyl)-5-iodo-2-indolinone 203990-73-2P,
     3-(2-Hydroxy-5-methoxybenzylidenyl)-5-iodo-2-indolinone
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. and testing of indolinone combinatorial library as protein
        kinase inhibitors)
     203990-74-3P, 3-[(Imidazol-2-yl)methylidenyl]-5-iodo-2-indolinone
ΙT
     203990-75-4P, 3-(2,4,6-Trifluorobenzylidenyl)-5-bromo-4-methyl-2-
     indolinone 203990-76-5P, 3-(4-Hydroxy-2-methoxybenzylidenyl)-5-
     bromo-4-methyl-2-indolinone 203990-77-6P, 3-(3,4-
     Dimethoxybenzylidenyl)-5-bromo-4-methyl-2-indolinone 203990-78-7P .
       3-(2-Hydroxybenzylidenyl)-5-bromo-4-methyl-2-indolinone
     203990-79-8P, 3-(Benzylidenyl)-5-bromo-4-methyl-2-indolinone
     203990-80-1P, 3-[[2-(Methylthio)thien-5-yl)methylidenyl]-5-bromo-4-.
     methyl-2-indolinone 203990-81-2P, 3-(2,4-Dihydroxy-6-
     methylbenzylidenyl)-5-bromo-4-methyl-2-indolinone 203990-82-3P,
     3-(3-Ethoxy-4-hydroxybenzylidenyl)-5-bromo-4-methyl-2-indolinone
     203990-83-4P, 3-(2-Hydroxy-5-methoxybenzylidenyl)-5-bromo-4-methyl-
     2-indolinone 203990-84-5P, 3-[(Imidazol-2-yl)methylidenyl]-5-
     bromo-4-methyl-2-indolinone 203990-85-6P,
     3-(2,4,6-Trifluorobenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
     203990-86-7P, 3-(4-Hydroxy-2-methoxybenzylidenyl)-5-
     [(methylamino)sulfonyl]-2-indolinone 203990-87-8P,
     3-(3,4-Dimethoxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
     203990-88-9P, 3-(2-Hydroxybenzylidenyl)-5-[(methylamino)sulfonyl]-
     2-indolinone 203990-89-0P, 3-(Benzylidenyl)-5-
     (methylamino) sulfonyl]-2-indolinone 203990-90-3P,
     3-[[2-(Methylthio)thien-5-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
     indolinone 203990-91-4P, 3-(2,4-Dihydroxy-6-methylbenzylidenyl)-
     5-[(methylamino)sulfonyl]-2-indolinone 203990-92-5P,
     3-(3-Ethoxy-4-hydroxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
     203990-93-6P, 3-(2-Hydroxy-5-methoxybenzylidenyl)-5-
     [(methylamino)sulfonyl]-2-indolinone 203990-94-7P,
     3-[(Imidazol-2-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
     203990-96-9P, 3-(2,4,6-Trifluorobenzylidenyl)-5-[[[4-
     (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203990-98-1P
       3-(4-Hydroxy-2-methoxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino
     [sulfonyl]-2-indolinone 203991-00-8P, 3-(3,4-
     Dimethoxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
     indolinone 203991-02-0P, 3-(2-Hydroxybenzylidenyl)-5-[[[4-
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(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203991-04-2P
, 3-(Benzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203991-05-3P, 3-[[2-(Methylthio)thien-5-
yl)methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
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203991-10-0P, 3-(3-Ethoxy-4-hydroxybenzylidenyl)-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203991-13-3P
  3-(2-Hydroxy-5-methoxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino
]sulfonyl]-2-indolinone 203991-16-6P, 3-[(Imidazol-2-
y1)methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
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3-(4-Hydroxy-2-methoxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
203991-27-9P, 3-(3,4-Dimethoxybenzylidenyl)-5-(morpholinosulfonyl)-
2-indolinone 203991-31-5P, 3-(2-Hydroxybenzylidenyl)-5-
(morpholinosulfonyl)-2-indolinone 203991-32-6P,
3-(Benzylidenyl)-5-(morpholinosulfonyl)-2-indolinone 203991-33-7P
  3-[[2-(Methylthio)thien-5-yl)methylidenyl]-5-(morpholinosulfonyl)-2-
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5-(morpholinosulfonyl)-2-indolinone 203991-35-9P,
3-(3-Ethoxy-4-hydroxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
203991-37-1P, 3-(2-Hydroxy-5-methoxybenzylidenyl)-5-
(morpholinosulfonyl) -2-indolinone 203991-39-3P,
3-[(Imidazol-2-yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone
203991-41-7P, 3-(2,4,6-Trifluorobenzylidenyl)-5-(2-chloroethyl)-2-
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Dimethoxybenzylidenyl)-5-(2-chloroethyl)-2-indolinone 203991-47-3P
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203991-49-5P, 3-(Benzylidenyl)-5-(2-chloroethyl)-2-indolinone
203991-51-9P, 3-[[2-(Methylthio)thien-5-yl)methylidenyl]-5-(2-
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203991-54-2P, 3-(2-Hydroxy-5-methoxybenzylidenyl)-5-(2-
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203991-57-5P, 3-[(4-Chloro-1-methylpyrazol-3-yl)methylidenyl]-5,7-
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3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5,7-dibromo-2-indolinone
203991-60-0P, 3-[3-(Chloromethyl)-2-hydroxy-5-nitrobenzylidenyl]-
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yl) methylidenyl]-5,7-dibromo-2-indolinone 203991-62-2P,
3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5,7-dibromo-2-indolinone
203991-63-3P, 3-(3-tert-Butyl-4-hydroxybenzylidenyl)-5,7-dibromo-2-
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203991-66-6P, 3-[(1-Methylbenzimidazol-2-yl)methylidenyl]-5-iodo-2-
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3-{(2,3-Dimethylthien-5-yl)methylidenyl]-5-iodo-2-indolinone
203991-69-9P, 3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5-
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3-[(2-Chlorothien-5-yl)methylidenyl]-5-iodo-2-indolinone
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203991-72-4P, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-iodo-2-
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5-iodo-2-indolinone 203991-74-6P, 3-(3-Bromo-5-tert-butyl-4-
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3-(3,5-Di-tert-butyl-4-hydroxybenzylidenyl)-5-iodo-2-indolinone
203991-76-8P, 3-[(1-Methylbenzimidazol-2-yl)methylidenyl]-5-bromo-
4-methyl-2-indolinone 203991-77-9P, 3-[(4-Chloro-1-methylpyrazol-
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203991-79-1P, 3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5-
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203991-81-5P, 3-[(2-Chlorothien-5-yl)methylidenyl]-5-bromo-4-
methyl-2-indolinone 203991-82-6P, 3-[(2,4-Dimethylpyrrol-5-
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203991-84-8P, 3-(3-Bromo-5-tert-butyl-4-hydroxybenzylidenyl)-5-
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hydroxybenzylidenyl)-5-bromo-4-methyl-2-indolinone 203991-86-0P,
 3-[\ (1-Methylbenzimidazol-2-yl)\,methylidenyl]-5-[\ (methylamino)\,sulfonyl]-2-line (1-Methylbenzimidazol-2-yl)\,methylidenyl]-1-line (1-Methylbenzimidazol-2-yl)\,methylidenylla (1-Methylbenzimidazol-2-yl)\,methylidenylla (1-Methylbenzimidazol-2-yl)\,methylla (1-Methylbenzimidazol-2-yl)\,methylla (1-Methylbenzimidazol-2-yl)\,methylla (1-Methylbenzimidazol-2-yl)\,methylla (1-Methylbenzimidazol-2-yl)\,methylla (1-Methylbenzimidazol-2-yl)\,methylla (1-Methylbenzimidazol-2-yl)\,methyll
indolinone 203991-87-1P, 3-[(4-Chloro-1-methylpyrazol-3-
y1)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203991-88-2P, 3-[(2,3-Dimethylthien-5-yl)methylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 203991-89-3P,
3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
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203991-91-7P, 3-[(2-Chlorothien-5-yl)methylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 203991-92-8P,
3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
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5-[(methylamino)sulfonyl]-2-indolinone 203991-94-0P,
3-(3-Bromo-5-tert-butyl-4-hydroxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-
indolinone 203991-95-1P, 3-(3,5-Di-tert-butyl-4-
hydroxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
203991-96-2P, 3-[(1-Methylbenzimidazol-2-yl)methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203991-97-3P
   3-[(4-Chloro-1-methylpyrazol-3-yl)methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203991-98-4P
   3-[(2,3-Dimethylthien-5-yl)methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203991-99-5P
   3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203992-00-1P
  3-[3-(Chloromethyl)-2-hydroxy-5-nitrobenzylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203992-01-2P
  3-[(2-Chlorothien-5-yl)methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203992-02-3P
  3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203992-03-4P
  3-(3-tert-Butyl-4-hydroxybenzylidenyl)-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203992-04-5P
, 3-(3-Bromo-5-tert-butyl-4-hydroxybenzylidenyl)-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203992-05-6P
, 3-(3,5-Di-tert-butyl-4-hydroxybenzylidenyl)-5-[[[4-
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   3-[(1-Methylbenzimidazol-2-yl)methylidenyl]-5-(morpholinosulfonyl)-2-
indolinone 203992-07-8P, 3-[(4-Chloro-1-methylpyrazol-3-
yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203992-08-9P
, 3-[(2,3-Dimethylthien-5-yl)methylidenyl]-5-(morpholinosulfonyl)-2-
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(morpholinosulfonyl)-2-indolinone 203992-11-4P,
3-[(2-Chlorothien-5-yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone
203992-12-5P, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-
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203992-14-7P, 3-(3-Bromo-5-tert-butyl-4-hydroxybenzylidenyl)-5-
(morpholinosulfonyl)-2-indolinone 203992-15-8P,
3-(3,5-Di-tert-butyl-4-hydroxybenzylidenyl)-5-(morpholinosulfonyl)-2-
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3-[(4-Chloro-1-methylpyrazol-3-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone 203992-18-1P, <math>3-[(2,3-Dimethylthien-5-
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3-[(4,5,6,7-Tetrahydroindol-2-yl)methylidenyl]-5-(2-chloroethyl)-2-
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3-[(2-Chlorothien-5-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
203992-22-7P, 3-[(2,4-Dimethylpyrrol-5-yl)methylidenyl]-5-(2-yl)methylidenyl]
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  3-(3-Bromo-5-tert-butyl-4-hydroxybenzylidenyl)-5-(2-chloroethyl)-2-
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hydroxybenzylidenyl)-5-(2-chloroethyl)-2-indolinone 203992-26-1P
  3-(3-tert-Butyl-4-hydroxy-5-nitrobenzylidenyl)-5,7-dibromo-2-indolinone
203992-27-2P, 3-(2,4,6-Trihydroxybenzylidenyl)-5,7-dibromo-2-
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5,7-dibromo-2-indolinone 203992-31-8P, 3-(3,5-Dimethyl-4-
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203992-33-0P, 3-[(2-Nitrothien-4-yl)methylidenyl]-5,7-dibromo-2-
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203992-36-3P, 3-(3-\text{tert-Butyl}-4-\text{hydroxy}-5-\text{nitrobenzylidenyl})-5-
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5-iodo-2-indolinone 203992-38-5P, 3-[(2-Nitrothien-5-
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3-(4-Carboxybenzylidenyl)-5-iodo-2-indolinone 203992-40-9P,
3-(2,4-Difluorobenzylidenyl)-5-iodo-2-indolinone 203992-41-0P,
3-(3,5-Dimethyl-4-hydroxybenzylidenyl)-5-iodo-2-indolinone
203992-42-1P, 3-(3-tert-Butyl-5-chloro-4-hydroxybenzylidenyl)-5-
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3-[4-(Di-n-butylamino)benzylidenyl]-5-iodo-2-indolinone
203992-45-4P, 3-[4-(Trifluoromethyl)benzylidenyl]-5-iodo-2-
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3-(2,4,6-Trihydroxybenzylidenyl)-5-bromo-4-methyl-2-indolinone
203992-48-7P, 3-[(2-Nitrothien-5-yl)methylidenyl]-5-bromo-4-methyl-
2-indolinone 203992-49-8P, 3-(4-Carboxybenzylidenyl)-5-bromo-4-
methyl-2-indolinone 203992-50-1P, 3-(2,4-Difluorobenzylidenyl)-5-
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hydroxybenzylidenyl)-5-bromo-4-methyl-2-indolinone 203992-52-3P,
3-(3-tert-Butyl-5-chloro-4-hydroxybenzylidenyl)-5-bromo-4-methyl-2-
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butylamino)benzylidenyl]-5-bromo-4-methyl-2-indolinone
203992-55-6P, 3-[4-(Trifluoromethyl)benzylidenyl]-5-bromo-4-methyl-
2-indolinone 203992-56-7P, 3-(3-tert-Butyl-4-hydroxy-5-
nitrobenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
203992-57-8P, 3-(2,4,6-Trihydroxybenzylidenyl)~5-
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203992-59-0P, 3-(4-Carboxybenzylidenyl)-5-[(methylamino)sulfonyl]-
2-indolinone 203992-60-3P, 3-(2,4-Difluorobenzylidenyl)-5-
[(methylamino)sulfonyl]-2-indolinone 203992-61-4P,
3-(3,5-Dimethyl-4-hydroxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-
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203992-63-6P, 3-[(2-Nitrothien-4-yl)methylidenyl]-5-
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3-[4-(Di-n-butylamino)benzylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203992-65-8P, 3-[4-(Trifluoromethyl)benzylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 203992-66-9P,
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                    ***203992-68-1P, 3-[(2-Nitrothien-5-
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yl)methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
indolinone 203992-69-2P, 3-(4-Carboxybenzylidenyl)-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203992-70-5P
  3-(2,4-Difluorobenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfon
yl]-2-indolinone 203992-71-6P, 3-(3,5-Dimethyl-4-
hydroxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
indolinone 203992-72-7P, 3-(3-tert-Butyl-5-chloro-4-
hydroxybenzylidenyl) -5 - \hbox{\tt [[\{4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-}\\
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  3-[4-(Trifluoromethyl)benzylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino
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203992-77-2P, 3-(2,4,6-Trihydroxybenzylidenyl)-5-
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3-[(2-Nitrothien-5-yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone
203992-79-4P, 3-(4-Carboxybenz\hat{y}lidenyl)-5-(morpholinosulfonyl)-2-
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3-(3,5-Dimethyl-4-hydroxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
203992-82-9P, 3-(3-tert-Butyl-5-chloro-4-hydroxybenzylidenyl)-5-
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203992-84-1P, 3-[4-(Di-n-butylamino)benzylidenyl]-5-
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203993-14-0P, 3-(3-Bromobenzylidenyl)-5-iodo-2-indolinone
203993-15-1P, 3-(3,5-Di-tert-butyl-2-hydroxybenzylidenyl)-5-iodo-2-
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203993-19-5P, 3-(3,4-Diacetoxybenzylidenyl)-5-bromo-4-methyl-2-
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203993-21-9P, 3-(2,4-Dihydroxybenzylidenyl)-5-bromo-4-methyl-2-
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Bromobenzylidenyl)-5-bromo-4-methyl-2-indolinone 203993-24-2P,
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203993-25-3P, 3-(2,3,4-Trihydroxybenzylidenyl)-5-
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3-(2-Hydroxy-3-methoxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
203993-27-5P, 3-(3-Bromo-4,5-dihydroxybenzylidenyl)-5-
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203993-29-7P, 3-(4-Hydroxy-3-methylbenzylidenyl)-5-
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3-(2-Bromobenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
203993-31-1P, 3-(2,4-Dihydroxybenzylidenyl)-5-
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3-(2-Hydroxy-4-methoxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
203993-33-3P, 3-(3-Bromobenzylidenyl)-5-[(methylamino)sulfonyl]-2-
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hydroxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
203993-35-5P, 3-(2,3,4-Trihydroxybenzylidenyl)-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203993-36-6P
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, 3-(2-Hydroxy-3-methoxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino
     ]sulfonyl]-2-indolinone 203993-37-7P, 3-(3-Bromo-4,5-
    dihydroxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203993-38-8P, 3-(3,4-Diacetoxybenzylidenyl)-5-[[[4-
     (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203993-39-9P
       3-(4-Hydroxy-3-methylbenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]
     sulfonyl]-2-indolinone
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. and testing of indolinone combinatorial library as protein
        kinase inhibitors)
     203993-40-2P, 3-(2-Bromobenzylidenyl)-5-[[[4-
ΙT
     (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203993-41-3P
       3-(2,4-Dihydroxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfo
     nyl]-2-indolinone 203993-42-4P, 3-(2-Hydroxy-4-
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     indolinone 203993-43-5P, 3-(3-Bromobenzylidenyl)-5-[[[4-
     (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203993-44-6P
       3-(3,5-Di-tert-butyl-2-hydroxybenzylidenyl)-5-[[[4-
     (\verb|trifluoromethyl|) phenyl| amino| sulfonyl| -2-indolinone | \textbf{203993-45-7P}|
       3-(2,3,4-Trihydroxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
     203993-46-8P, 3-(2-Hydroxy-3-methoxybenzylidenyl)-5-
     (morpholinosulfonyl)-2-indolinone 203993-47-9P,
     3-(3-Bromo-4,5-dihydroxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
     203993-48-0P, 3-(3,4-Diacetoxybenzylidenyl)-5-(morpholinosulfonyl)-
     2-indolinone 203993-49-1P, 3-(4-Hydroxy-3-methylbenzylidenyl)-5-
     (morpholinosulfonyl)-2-indolinone 203993-50-4P,
     3-(2-Bromobenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
     203993-51-5P, 3-(2,4-Dihydroxybenzylidenyl)-5-(morpholinosulfonyl)-
     2-indolinone 203993-52-6P, 3-(2-Hydroxy-4-methoxybenzylidenyl)-5-
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     203993-59-3P, 3-(4-Hydroxy-3-methylbenzylidenyl)-5-(2-chloroethyl)-
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     203993-63-9P, 3-(3-Bromobenzylidenyl)-5-(2-chloroethyl)-2-
     indolinone 203993-64-0P, 3-(3,5-Di-tert-butyl-2-
     hydroxybenzylidenyl)-5-(2-chloroethyl)-2-indolinone 203993-65-1P
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     203993-66-2P, 3-(4-Hydroxy-3-nitrobenzylidenyl)-5,7-dibromo-2-
     indolinone 203993-67-3P, 3-(3-Hydroxy-4-nitrobenzylidenyl)-5,7-
     dibromo-2-indolinone 203993-68-4P, 3-[(8-Hydroxy-2,3,6,7-
     tetrahydro-1H,5H-benzo[ij]quinolizin-9-yl)methylidenyl]-5,7-dibromo-2-
     indolinone 203993-69-5P, 3-(3,5-Diisopropyl-4-
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     3-[(Benzo[b]furan-2-yl)methylidenyl]-5,7-dibromo-2-indolinone
     203993-71-9P, 3-[[1-(4-Chlorophenyl)pyrrol-2-yl]methylidenyl]-5,7-
     dibromo-2-indolinone 203993-72-0P, 3-[(2-Ethylfuran-5-
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3-[(3,4-Dimethylthieno[2,3-b]thien-2-yl)methylidenyl]-5,7-dibromo-2-
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yl)methylidenyl]-5-iodo-2-indolinone 203993-75-3P,
3-(4-Hydroxy-3-nitrobenzylidenyl)-5-iodo-2-indolinone 203993-76-4P
   3-(3-Hydroxy-4-nitrobenzylidenyl)-5-iodo-2-indolinone
203993-77-5P, 3-[(8-Hydroxy-2,3,6,7-tetrahydro-1H,5H-
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203993-78-6P, 3-(3,5-Diisopropyl-4-hydroxybenzylidenyl)-5-iodo-2-
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203993-82-2P, 3-[(3,4-Dimethylthieno[2,3-b]thien-2-
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203993-88-8P, 3-[(Benzo[b]furan-2-yl)methylidenyl]-5-bromo-4-
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203994-61-0P, 3-(2-Bromo-6-hydroxy-5-methoxybenzylidenyl)-5-bromo-
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 3-[4-(4-Formylpiperazin-1-yl)benzylidenyl]-5-[[[4-
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  3-[4-(Morpholino)benzylidenyl]-5-(morpholinosulfonyl)-2-indolinone
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      203995-33-9P, 3-(2-Hydroxy-6-methoxy-4-methylbenzylidenyl)-5-(2-
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      3-[4-(Morpholino)benzylidenyl]-5-(2-chloroethyl)-2-indolinone
      203995-36-2P, 3-[[2-Chloro-4-(methoxycarbonyl)-3-
      \label{lem:condition} \begin{tabular}{ll} $(methoxycarbonyl)$ methyl] pyrrol-5-yl] $methylidenyl]-5-(2-chloroethyl)-2-lem (and the condition of the condition
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    3-(4-Methoxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-
2-indolinone 203995-84-0P, 3-[[2-(Ethoxycarbonyl)-4-
(methoxycarbonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] methylidenyl] - 5 - (morpholinosulfonyl) - 3 - methylpyrrol - 5 - yl] - 5 - (morpholinosulfonyl) - 3 - yl] - yl] - 3 - yl] - 3 - yl] - yl
2-indolinone 203995-85-1P, 3-(3-tert-Butyl-4-hydroxy-5-
methylbenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
203995-86-2P, 3-[(2-Bromofuran-5-yl)methylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 203995-87-3P,
3-[(1,3-Dimethylpyrrol-4-yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203995-88-4P, <math>3-[(5,8-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,3,4-Dihydroxy-1,2,4,4-Dihydroxy-1,2,4,4-Dihydroxy-1,2,4,4-Dihydroxy-1,2,4,4-Dihydroxy-1,2,4,4
tetrahydronaphth-6-yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone
203995-89-5P 203995-90-8P 203995-91-9P,
3-[(2-Ethylthien-5-yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone
203995-92-0P, 3-(4-Methoxybenzylidenyl)-5-(morpholinosulfonyl)-2-
indolinone 203995-93-1P, 3-[[2-(Ethoxycarbonyl)-4-
(methoxycarbonyl)-3-methylpyrrol-5-yl]methylidenyl]-5-(2-chloroethyl)-2-
indolinone 203995-94-2P, 3-(3-tert-Butyl-4-hydroxy-5-
methylbenzylidenyl)-5-(2-chloroethyl)-2-indolinone 203995-95-3P,
3-[(2-Bromofuran-5-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
203995-96-4P, 3-[(1,3-Dimethylpyrrol-4-yl)methylidenyl]-5-(2-
chloroethyl) -2-indolinone 203995-97-5P, 3-[(5,8-Dihydroxy-
1,2,3,4-tetrahydronaphth-6-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
203995-98-6P .203995-99-7P 203996-00-3P,
3-[(2-Ethylthien-5-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
203996-01-4P, 3-(4-Methoxybenzylidenyl)-5-(2-chloroethyl)-2-
indolinone 203996-02-5P, 3-[4-(Diethylamino)benzylidenyl]-5,7-
dibromo-2-indolinone 203996-03-6P, 3-[(2,4-Diethylpyrrol-5-
yl)methylidenyl]-5,7-dibromo-2-indolinone 203996-04-7P,
3-(3-Bromo-5-chloro-2-hydroxybenzylidenyl)-5,7-dibromo-2-indolinone
203996-05-8P, 3-[2-[(4-Chlorophenyl)thio]benzylidenyl]-5,7-dibromo-
2-indolinone 203996-06-9P, 3-[(5-Chlorobenzodioxolan-6-
yl)methylidenyl]-5,7-dibromo-2-indolinone 203996-07-0P,
3-[(1,4-Benzopyranon-3-yl)methylidenyl]-5,7-dibromo-2-indolinone
203996-08-1P, 3-(3-Cyanobenzylidenyl)-5,7-dibromo-2-indolinone
203996-09-2P, 3-(4-Cyanobenzylidenyl)-5,7-dibromo-2-indolinone
203996-10-5P, 3-(2,5-Dihydroxybenzylidenyl)-5,7-dibromo-2-
indolinone 203996-11-6P, 3-(2,3-Dimethoxybenzylidenyl)-5,7-
dibromo-2-indolinone 203996-12-7P, 3-[4-
(Diethylamino)benzylidenyl]-5-iodo-2-indolinone 203996-13-8P,
3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-iodo-2-indolinone
203996-14-9P, 3-(3-Bromo-5-chloro-2-hydroxybenzylidenyl)-5-iodo-2-
indolinone 203996-15-0P, 3-[2-[(4-Chlorophenyl)thio]benzylidenyl
]-5-iodo-2-indolinone
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RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
    preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. and testing of indolinone combinatorial library as protein
        kinase inhibitors)
     203996-16-1P, 3-[(5-Chlorobenzodioxolan-6-yl)methylidenyl]-5-iodo-
ΙT
     2-indolinone 203996-17-2P, 3-[(1,4-Benzopyranon-3-
     yl)methylidenyl]-5-iodo-2-indolinone 203996-18-3P,
     3-(3-Cyanobenzylidenyl)-5-iodo-2-indolinone 203996-19-4P,
     3-(4-Cyanobenzylidenyl)-5-iodo-2-indolinone 203996-20-7P,
     3-(2,5-Dihydroxybenzylidenyl)-5-iodo-2-indolinone 203996-21-8P,
     3-(2,3-Dimethoxybenzylidenyl)-5-iodo-2-indolinone 203996-22-9P,
     3-[4-(Diethylamino)benzylidenyl]-5-bromo-4-methyl-2-indolinone
     203996-23-0P, 3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-bromo-4-
     methyI-2-indolinone 203996-24-1P, 3-(3-Bromo-5-chloro-2-
     hydroxybenzylidenyl)-5-bromo-4-methyl-2-indolinone 203996-25-2P,
     3-[2-[(4-Chlorophenyl)thio]benzylidenyl]-5-bromo-4-methyl-2-indolinone
     203996-26-3P, 3-[(5-Chlorobenzodioxolan-6-yl)methylidenyl]-5-bromo-
     4-methyl-2-indolinone 203996-27-4P, 3-[(1,4-Benzopyranon-3-
     yl)methylidenyl]-5-bromo-4-methyl-2-indolinone 203996-28-5P,
     3-(3-Cyanobenzylidenyl)-5-bromo-4-methyl-2-indolinone 203996-29-6P
       3-(4-Cyanobenzylidenyl)-5-bromo-4-methyl-2-indolinone
     203996-30-9P, 3-(2,5-Dihydroxybenzylidenyl)-5-bromo-4-methyl-2-
     indolinone 203996-31-0P, 3-(2,3-Dimethoxybenzylidenyl)-5-bromo-4-
     methyl-2-indolinone 203996-32-1P, 3-[4-
     (Diethylamino)benzylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
     203996-33-2P, 3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-
     [(methylamino)sulfonyl]-2-indolinone 203996-34-3P,
     3-(3-Bromo-5-chloro-2-hydroxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-
     indolinone 203996-35-4P, 3-[2-[(4-Chlorophenyl)thio]benzylidenyl
     ]-5-[(methylamino)sulfonyl]-2-indolinone 203996-36-5P,
     3-[(5-Chlorobenzodioxolan-6-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
     indolinone 203996-37-6P, 3-[(1,4-Benzopyranon-3-yl)methylidenyl]-
     5-[(methylamino)sulfonyl]-2-indolinone 203996-38-7P,
     3-(3-Cyanobenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
     203996-39-8P, 3-(4-Cyanobenzylidenyl)-5-[(methylamino)sulfonyl]-2-
     indolinone 203996-40-1P, 3-(2,5-Dihydroxybenzylidenyl)-5-
     [(methylamino)sulfonyl]-2-indolinone 203996-41-2P,
     3-(2,3-Dimethoxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
     203996-42-3P, 3-[4-(Diethylamino)benzylidenyl]-5-[[[4-
     (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203996-43-4P
       3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-[[[4-
     (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203996-44-5P
       3-(3-Bromo-5-chloro-2-hydroxybenzylidenyl)-5-[[[4-
     (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203996-45-6P
     , 3-[2-[(4-Chlorophenyl)thio]benzylidenyl]-5-[[[4-
     (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203996-46-7P
     , 3-[(5-Chlorobenzodioxolan-6-yl)methylidenyl]-5-[[[4-
     (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203996-47-8P
     , 3-[(1,4-Benzopyranon-3-yl)methylidenyl]-5-[[[4-
     (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203996-48-9P
       3-(3-Cyanobenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
     indolinone 203996-49-0P, 3-(4-Cyanobenzylidenyl)-5-[[[4-
     (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203996-50-3P
       3-(2,5-Dihydroxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfo
     nyl]-2-indolinone 203996-51-4P, 3-(2,3-Dimethoxybenzylidenyl)-5-
     [[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
     203996-52-5P, 3-[4-(Diethylamino)benzylidenyl]-5-
     (morpholinosulfonyl)-2-indolinone 203996-53-6P,
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3-[(2,4-Diethylpyrrol-5-yl)methylidenyl]-5-(morpholinosulfonyl)-2-
indolinone 203996-54-7P, 3-(3-Bromo-5-chloro-2-
hydroxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
203996-55-8P, 3-[2-[(4-Chlorophenyl)thio]benzylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 203996-56-9P,
3-{(5-Chlorobenzodioxolan-6-yl)methylidenyl}-5-(morpholinosulfonyl)-2-
indolinone 203996-57-0P, 3-[(1,4-Benzopyranon-3-yl)methylidenyl]-
5-(morpholinosulfonyl)-2-indolinone 203996-58-1P,
3-(3-Cyanobenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
203996-59-2P, 3-(4-Cyanobenzylidenyl)-5-(morpholinosulfonyl)-2-
indolinone 203996-60-5P, 3-(2,5-Dihydroxybenzylidenyl)-5-
(morpholinosulfonyl)-2-indolinone 203996-61-6P,
3-(2,3-Dimethoxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
203996-62-7P, 3-[4-(Diethylamino)benzylidenyl]-5-(2-chloroethyl)-2-
indolinone 203996-63-8P, 3-[(2,4-Diethylpyrrol-5-
yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone 203996-64-9P,
3-(3-Bromo-5-chloro-2-hydroxybenzylidenyl)-5-(2-chloroethyl)-2-indolinone
203996-65-0P, 3-[2-[(4-Chlorophenyl)thio]benzylidenyl]-5-(2-
chloroethyl)-2-indolinone 203996-66-1P, 3-[(5-
Chlorobenzodioxolan-6-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
203996-67-2P, 3-[(1,4-Benzopyranon-3-yl)methylidenyl]-5-(2-
chloroethyl)-2-indolinone 203996-68-3P, 3-(3-Cyanobenzylidenyl)-
5-(2-chloroethyl)-2-indolinone 203996-69-4P,
3-(4-Cyanobenzylidenyl)-5-(2-chloroethyl)-2-indolinone
203996-70-7P, 3-(2,5-Dihydroxybenzylidenyl)-5-(2-chloroethyl)-2-
indolinone 203996-71-8P, 3-(2,3-Dimethoxybenzylidenyl)-5-(2-
chloroethyl)-2-indolinone 203996-72-9P, 3-(2,5-
Dimethoxybenzylidenyl)-5,7-dibromo-2-indolinone 203996-73-0P,
3-(2,6-Dimethoxybenzylidenyl)-5,7-dibromo-2-indolinone
203996-74-1P, 3-(3,5-Dimethoxybenzylidenyl)-5,7-dibromo-2-
indolinone 203996-75-2P, 3-[4-(Dimethylamino)-2-
methoxybenzylidenyl]-5,7-dibromo-2-indolinone 203996-76-3P,
3-[(Fluoren-2-yl)methylidenyl]-5,7-dibromo-2-indolinone
203996-77-4P, 3-[2-Fluoro-3-(trifluoromethyl)benzylidenyl]-5,7-
dibromo-2-indolinone 203996-78-5P, 3-[2-Fluoro-5-
(\verb|trifluoromethyl|) benzylidenyl] -5, 7-dibromo-2-indolinone
203996-79-6P, 3-[2-Fluoro-6-(trifluoromethyl)benzylidenyl]-5,7-
dibromo-2-indolinone 203996-80-9P, 3-[2-
(Carboxymethoxy)benzylidenyl]-5,7-dibromo-2-indolinone
203996-81-0P, 3-[(4-Methoxybenzodioxolan-6-yl)methylidenyl]-5,7-
dibromo-2-indolinone 203996-82-1P, 3-(2,5-Dimethoxybenzylidenyl)-
5-iodo-2-indolinone 203996-83-2P, 3-(2,6-Dimethoxybenzylidenyl)-
5-iodo-2-indolinone 203996-84-3P, 3-(3,5-Dimethoxybenzylidenyl)-
5-iodo-2-indolinone 203996-85-4P, 3-[4-(Dimethylamino)-2-
methoxybenzylidenyl]-5-iodo-2-indolinone 203996-86-5P,
3-[(Fluoren-2-y1)methylidenyl]-5-iodo-2-indolinone 203996-87-6P,
3-[2-Fluoro-3-(trifluoromethyl)benzylidenyl]-5-iodo-2-indolinone
203996-88-7P, 3-[2-Fluoro-5-(trifluoromethyl)benzylidenyl]-5-iodo-
2-indolinone 203996-89-8P, 3-[2-Fluoro-6-
(trifluoromethyl)benzylidenyl]-5-iodo-2-indolinone 203996-90-1P,
3-[2-(Carboxymethoxy)benzylidenyl]-5-iodo-2-indolinone
203996-91-2P, 3-{(4-Methoxybenzodioxolan-6-yl)methylidenyl]-5-iodo-
2-indolinone 203996-92-3P, 3-(2,5-Dimethoxybenzylidenyl)-5-bromo-
4-methyl-2-indolinone 203996-93-4P, 3-(2,6-
Dimethoxybenzylidenyl)-5-bromo-4-methyl-2-indolinone 203996-94-5P
  3-(3,5-Dimethoxybenzylidenyl)-5-bromo-4-methyl-2-indolinone
203996-95-6P, 3-[4-(Dimethylamino)-2-methoxybenzylidenyl]-5-bromo-
4-methyl-2-indolinone 203996-96-7P, 3-[(Fluoren-2-
yl)methylidenyl]-5-bromo-4-methyl-2-indolinone 203996-97-8P,
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3-[2-Fluoro-3-(trifluoromethyl)benzylidenyl]-5-bromo-4-methyl-2-indolinone
203996-98-9P, 3-[2-Fluoro-5-(trifluoromethyl)benzylidenyl]-5-bromo-
4-methyl-2-indolinone 203996-99-0P, 3-[2-Fluoro-6-
(\verb|trifluoromethyl|) \verb|benzylidenyl|] - 5 - \verb|bromo-4-methyl-2-indolinone|
203997-00-6P, 3-[2-(Carboxymethoxy)benzylidenyl]-5-bromo-4-methyl-
2-indolinone 203997-01-7P, 3-[(4-Methoxybenzodioxolan-6-
yl)methylidenyl]-5-bromo-4-methyl-2-indolinone 203997-02-8P,
3-(2,5-Dimethoxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
203997-03-9P, 3-(2,6-Dimethoxybenzylidenyl)-5-
[(methylamino)sulfonyl]-2-indolinone 203997-04-0P,
3-(3,5-Dimethoxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
203997-05-1P, 3-[4-(Dimethylamino)-2-methoxybenzylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 203997-06-2P,
 3- \hbox{\tt [(Fluoren-2-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone } \\
203997-07-3P, 3-[2-Fluoro-3-(trifluoromethyl)benzylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 203997-08-4P,
3-[2-Fluoro-5-(trifluoromethyl)benzylidenyl]-5-[(methylamino)sulfonyl]-2-
indolinone 203997-09-5P, 3-[2-Fluoro-6-
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203997-10-8P, 3-[2-(Carboxymethoxy)benzylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 203997-11-9P,
3-[(4-Methoxybenzodioxolan-6-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
indolinone 203997-12-0P, 3-(2,5-Dimethoxybenzylidenyl)-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203997-13-1P
, 3-(2,6-Dimethoxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203997-14-2P, 3-(3,5-Dimethoxybenzylidenyl)-5-
[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
203997-15-3P, 3-[4-(Dimethylamino)-2-methoxybenzylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203997-16-4P
, 3-[(Fluoren-2-yl)methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203997-17-5P, 3-[2-Fluoro-3-
(trifluoromethyl)benzylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfon
yl]-2-indolinone 203997-18-6P, 3-[2-Fluoro-5-
(\verb|trifluoromethyl|) \verb|benzylidenyl|] - 5 - [[[4 - (\verb|trifluoromethyl|) phenyl] amino] sulfon
yl]-2-indolinone 203997-19-7P, 3-[2-Fluoro-6-
(\verb|trifluoromethyl|) benzylidenyl] -5 - [[[4 - (\verb|trifluoromethyl|) phenyl] amino] sulfon
yl]-2-indolinone 203997-20-0P, 3-[2-
(Carboxymethoxy)benzylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfony
1]-2-indolinone 203997-21-1P, 3-[(4-Methoxybenzodioxolan-6-
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indolinone 203997-22-2P, 3-(2,5-Dimethoxybenzylidenyl)-5-
(morpholinosulfonyl)-2-indolinone 203997-23-3P,
3-(2,6-Dimethoxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
203997-24-4P, 3-(3,5-Dimethoxybenzylidenyl)-5-(morpholinosulfonyl)-
2-indolinone 203997-25-5P, 3-[4-(Dimethylamino)-2-
methoxybenzylidenyl]-5-(morpholinosulfonyl)-2-indolinone
203997-26-6P, 3-[(Fluoren-2-yl)methylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 203997-27-7P,
3-[2-Fluoro-3-(trifluoromethyl)benzylidenyl]-5-(morpholinosulfonyl)-2-
indolinone 203997-28-8P, 3-[2-Fluoro-5-
(trifluoromethyl)benzylidenyl]-5-(morpholinosulfonyl)-2-indolinone
203997-29-9P, 3-[2-Fluoro-6-(trifluoromethyl)benzylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 203997-30-2P,
 3-[2-(Carboxymethoxy)benzylidenyl]-5-(morpholinosulfonyl)-2-indolinone \\
203997-31-3P, 3-[(4-Methoxybenzodioxolan-6-yl)methylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 203997-32-4P,
3-(2,5-Dimethoxybenzylidenyl)-5-(2-chloroethyl)-2-indolinone
203997-33-5P, 3-(2,6-Dimethoxybenzylidenyl)-5-(2-chloroethyl)-2-
indolinone 203997-34-6P, 3-(3,5-Dimethoxybenzylidenyl)-5-(2-
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chloroethyl)-2-indolinone 203997-35-7P, 3-[4-(Dimethylamino)-2-
methoxybenzylidenyl]-5-(2-chloroethyl)-2-indolinone 203997-36-8P
  3-[(Fluoren-2-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
203997-37-9P, 3-[2-Fluoro-3-(trifluoromethyl)benzylidenyl]-5-(2-
chloroethyl)-2-indolinone 203997-38-0P, 3-[2-Fluoro-5-
(trifluoromethyl)benzylidenyl]-5-(2-chloroethyl)-2-indolinone
203997-39-1P, 3-[2-Fluoro-6-(trifluoromethyl)benzylidenyl]-5-(2-
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(Carboxymethoxy) benzylidenyl]-5-(2-chloroethyl)-2-indolinone
203997-41-5P, 3-[(4-Methoxybenzodioxolan-6-yl)methylidenyl]-5-(2-
chloroethyl)-2-indolinone 203997-42-6P, 3-[(2-Methoxynaphth-1-
y1) methylidenyl]-5,7-dibromo-2-indolinone 203997-43-7P,
3-[(1-Methoxynaphth-4-yl)methylidenyl]-5,7-dibromo-2-indolinone
203997-44-8P, 3-[4-(Methylthio)benzylidenyl]-5,7-dibromo-2-
indolinone 203997-45-9P, 3-[(3-Methylthien-2-yl)methylidenyl]-
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3-[(Pyrid-3-yl)methylidenyl]-5,7-dibromo-2-indolinone 203997-49-3P
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203997-54-0P, 3-[4-(Methylthio)benzylidenyl]-5-iodo-2-indolinone
203997-55-1P, 3-[(3-Methylthien-2-yl)methylidenyl]-5-iodo-2-
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indolinone 203997-58-4P, 3-[(Pyrid-3-yl)methylidenyl]-5-iodo-2-
indolinone 203997-59-5P, 3-[(Pyrid-4-yl)methylidenyl]-5-iodo-2-indolinone 203997-60-8P, 3-[4-(Pyrrolidin-1-yl)benzylidenyl]-5-
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203997-63-1P, 3-[(1-Methoxynaphth-4-yl)methylidenyl]-5-bromo-4-
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3-[(3-Methylthien-2-yl)methylidenyl]-5-bromo-4-methyl-2-indolinone
203997-66-4P, 3-(3-Phenoxybenzylidenyl)-5-bromo-4-methyl-2-
indolinone 203997-67-5P, 3-[(Pyrid-2-yl)methylidenyl]-5-bromo-4-
methyl-2-indolinone 203997-68-6P, 3-[(Pyrid-3-yl)methylidenyl]-5-
bromo-4-methyl-2-indolinone 203997-69-7P, 3-[(Pyrid-4-
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3-[4-(Pyrrolidin-1-yl)benzylidenyl]-5-bromo-4-methyl-2-indolinone
\textbf{203997-71-1P}, \quad 3-[(Cyclohexen-3-yl)methylidenyl]-5-bromo-4-methyl-2-
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5-[(methylamino)sulfonyl]-2-indolinone 203997-73-3P,
3-[(1-Methoxynaphth-4-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
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3-[(3-Methylthien-2-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
indolinone 203997-76-6P, 3-(3-Phenoxybenzylidenyl)-5-
[(methylamino)sulfonyl]-2-indolinone 203997-77-7P,
3-[(Pyrid-2-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203997-78-8P, 3-[(Pyrid-3-yl)methylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 203997-79-9P,
3-[(Pyrid-4-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203997-81-3P, 3-[4-(Pyrrolidin-1-yl)benzylidenyl]-5-
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   203997-85-7P, 3-[(2-Methoxynaphth-1-yl)methylidenyl]-5-[[[4-
    (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203997-87-9P
      3-[(1-Methoxynaphth-4-yl)methylidenyl]-5-[[[4-
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      3-[4-(Methylthio)benzylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulf
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   yl)methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
   indolinone 203997-91-5P, 3-(3-Phenoxybenzylidenyl)-5-[[[4-
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   203997-94-8P, 3-[(Pyrid-4-yl)methylidenyl]-5-[[[4-
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      3-[4-(Pyrrolidin-1-yl)benzylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino
   ]sulfonyl]-2-indolinone 203997-96-0P, 3-[(Cyclohexen-3-
   yl)methylidenyl]-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
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   203997-99-3P, 3-[4-(Methylthio)benzylidenyl]-5-
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   indolinone 203998-02-1P, 3-[(Pyrid-2-yl)methylidenyl]-5-
    (morpholinosulfonyl)-2-indolinone 203998-03-2P,
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    (morpholinosulfonyl)-2-indolinone 203998-06-5P,
   3-[(Cyclohexen-3-yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone
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   203998-13-4P, 3-[(Pyrid-3-yl)methylidenyl]-5-(2-chloroethyl)-2-
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   203998-17-8P, 3-(2,3,4-Trimethoxybenzylidenyl)-5,7-dibromo-2-
   indolinone 203998-18-9P, 3-(2,4,5-Trimethoxybenzylidenyl)-5,7-
   dibromo-2-indolinone 203998-19-0P, 3-(3,4,5-
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   3-[(1-Acetylindol-3-yl)methylidenyl]-5,7-dibromo-2-indolinone
   203998-21-4P, 3-{(6-Chloro-1,4-benzopyranon-3-yl)methylidenyl}-5,7-
   dibromo-2-indolinone 203998-22-5P
3-[[2-(2-Chlorophenyl)furan-5-yl]methylidenyl]-5,7-dibromo-2-indolinone
   203998-23-6P, 3-[(2-Chloroquinolin-3-yl)methylidenyl]-5,7-dibromo-
   2-indolinone 203998-24-7P, 3-[(6,8-Dibromo-1,4-benzopyranon-3-
   yl)methylidenyl]-5,7-dibromo-2-indolinone 203998-25-8P,
   3-[(2,5-Dimethoxytetrahydrofuran-3-yl)methylidenyl]-5,7-dibromo-2-
   indolinone 203998-26-9P, 3-[(2,3-Dimethylfuran-5-
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3-(2,3,4-Trimethoxybenzylidenyl)-5-iodo-2-indolinone 203998-28-1P
  3-(2,4,5-Trimethoxybenzylidenyl)-5-iodo-2-indolinone
203998-29-2P, 3-(3,4,5-Trimethoxybenzylidenyl)-5-iodo-2-indolinone
203998-30-5P, 3-[(1-Acetylindol-3-yl)methylidenyl]-5-iodo-2-
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203998-33-8P, 3-[(2-Chloroquinolin-3-yl)methylidenyl]-5-iodo-2-
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203998-36-1P, 3-[(2,3-Dimethylfuran-5-yl)methylidenyl]-5-iodo-2-
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Trimethoxybenzylidenyl)-5-bromo-4-methyl-2-indolinone 203998-39-4P
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3-[[2-(2-Chlorophenyl)furan-5-yl]methylidenyl]-5-bromo-4-methyl-2-
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5-bromo-4-methyl-2-indolinone 203998-44-1P, 3-[(6,8-Dibromo-1,4-
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203998-45-2P, 3-[(2,5-Dimethoxytetrahydrofuran-3-yl)methylidenyl]-
5-bromo-4-methyl-2-indolinone 203998-46-3P, 3-[(2,3-
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203998-47-4P, 3-(2,3,4-Trimethoxybenzylidenyl)-5-
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203998-49-6P, 3-(3,4,5-Trimethoxybenzylidenyl)-5-
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3-[(1-Acetylindol-3-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
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203998-52-1P, 3-[[2-(2-Chlorophenyl)furan-5-yl]methylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 203998-53-2P,
3-[(2-Chloroquinolin-3-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
indolinone 203998-54-3P, 3-[(6,8-Dibromo-1,4-benzopyranon-3-
y1) methylideny1]-5-[(methylamino) sulfony1]-2-indolinone
203998-55-4P, 3-[(2,5-Dimethoxytetrahydrofuran-3-yl)methylidenyl]-
5-[(methylamino)sulfonyl]-2-indolinone
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
preparation); THU (Therapeutic use); BIOL (Biological study); PREP
(Preparation); USES (Uses)
   (prepn. and testing of indolinone combinatorial library as protein
   kinase inhibitors)
203998-56-5P, 3-[(2,3-Dimethylfuran-5-yl)methylidenyl]-5-
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onyl]-2-indolinone 203998-58-7P, 3-(2,4,5-
Trimethoxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
indolinone 203998-59-8P, 3-(3,4,5-Trimethoxybenzylidenyl)-5-[[[4-
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, 3-[(1-Acetylindol-3-yl)methylidenyl]-5-[[[4-
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, 3-[(6-Chloro-1,4-benzopyranon-3-y1)methylideny1]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203998-62-3P
, 3-[[2-(2-Chlorophenyl)furan-5-yl]methylidenyl]-5-[[[4-
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3-(2,3,4-Trimethoxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
***203998-68-9P, 3-(2,4,5-Trimethoxybenzylidenyl)-5-
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3-(3,4,5-Trimethoxybenzylidenyl)-5-(morpholinosulfonyl)-2-indolinone
203998-70-3P, 3-[(1-Acetylindol-3-yl)methylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 203998-71-4P,
3-[(6-Chloro-1,4-benzopyranon-3-yl)methylidenyl]-5-(morpholinosulfonyl)-2-
indolinone 203998-72-5P, 3-[[2-(2-Chlorophenyl)furan-5-
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203998-87-2P, 3-[(9-Ethylcarbazol-3-yl)methylidenyl]-5,7-dibromo-2-
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3-[[4-(Propen-2-yl)cyclohexen-1-yl]methylidenyl]-5,7-dibromo-2-indolinone
203998-90-7P, 3-[(6-Isopropyl-1,4-benzopyron-3-yl)methylidenyl]-
5,7-dibromo-2-indolinone 203998-91-8P, 3-[(6-Methyl-1,4-
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203998-92-9P, 3-[(6-Nitro-1,4-benzopyron-3-yl)methylidenyl]-5,7-
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203998-95-2P 203998-96-3P, 3-[[2-(2-Nitrophenyl)furan-5-
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203999-01-3P, 3-[(6,7-Dimethyl-1,4-benzopyron-3-yl)methylidenyl]-5-
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3-[(6-Isopropyl-1,4-benzopyron-3-yl)methylidenyl]-5-iodo-2-indolinone
203999-04-6P, 3-[(6-Methyl-1,4-benzopyron-3-yl)methylidenyl]-5-
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3-[(Pyrimid-2,4-dion-5-yl)methylidenyl]-5-iodo-2-indolinone
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203999-10-4P, 3-[(9-Ethylcarbazol-3-yl)methylidenyl]-5-bromo-4-
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benzopyron-3-yl)methylidenyl]-5-bromo-4-methyl-2-indolinone
203999-12-6P, 3-[[4-(Propen-2-yl)cyclohexen-1-yl]methylidenyl]-5-
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203999-16-0P 203999-17-1P, 3-[(5-Methoxyindol-3-
yl)methylidenyl]-5-bromo-4-methyl-2-indolinone 203999-18-2P
203999-19-3P, 3-[[2-(2-Nitrophenyl)furan-5-yl]methylidene]-5-bromo-
4-methyl-2-indolinone 203999-20-6P, 3-[(9-Ethylcarbazol-3-
yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203999-21-7P, 3-[(6,7-Dimethyl-1,4-benzopyron-3-yl)methylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 203999-22-8P,
3-[[4-(Propen-2-y1)cyclohexen-1-y1]methylideny1]-5-[(methylamino)sulfony1]-
2-indolinone 203999-23-9P, 3-[(6-Isopropyl-1,4-benzopyron-3-
yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
203999-24-0P, 3-[(6-Methyl-1,4-benzopyron-3-yl)methylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 203999-25-1P,
3-[(6-Nitro-1,4-benzopyron-3-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
indolinone 203999-26-2P 203999-27-3P,
3-[(5-Methoxyindol-3-yl)methylidenyl]-5-[(methylamino)sulfonyl]-2-
indolinone 203999-28-4P 203999-29-5P,
3-[[2-(2-Nitrophenyl)furan-5-yl]methylidene]-5-[(methylamino)sulfonyl]-2-
indolinone 203999-30-8P, 3-[(9-Ethylcarbazol-3-yl)methylidenyl]-
5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
203999-31-9P, 3-[(6,7-Dimethyl-1,4-benzopyron-3-yl)methylidenyl]-5-
[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
203999-32-0P, 3-[[4-(Propen-2-yl)cyclohexen-1-yl]methylidenyl]-5-
[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
203999-33-1P, 3-[(6-Isopropyl-1,4-benzopyron-3-yl)methylidenyl]-5-
[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
\textbf{203999-36-4P}, \quad 3-[(6-Methyl-1,4-benzopyron-3-yl)methylidenyl]-5-
[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
203999-38-6P, 3-[(6-Nitro-1,4-benzopyron-3-yl)methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203999-40-0P
203999-42-2P, 3-[(5-Methoxyindol-3-yl)methylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203999-44-4P
203999-46-6P, 3-[[2-(2-Nitrophenyl)furan-5-yl]methylidene]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 203999-47-7P
 3-[(9-Ethylcarbazol-3-y1)methylidenyl]-5-(morpholinosulfonyl)-2-
indolinone 203999-48-8P, 3-[(6,7-Dimethyl-1,4-benzopyron-3-
yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203999-49-9P
 3-[[4-(Propen-2-yl)cyclohexen-1-yl]methylidenyl]-5-(morpholinosulfonyl)-
2-indolinone 203999-50-2P, 3-[(6-Isopropyl-1,4-benzopyron-3-
yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203999-51-3P
  3-[(6-Methyl-1,4-benzopyron-3-yl)methylidenyl]-5-(morpholinosulfonyl)-2-
indolinone 203999-52-4P, 3-[(6-Nitro-1,4-benzopyron-3-
yl)methylidenyl]-5-(morpholinosulfonyl)-2-indolinone 203999-53-5P
203999-54-6P, 3-[(5-Methoxyindol-3-yl)methylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 203999-55-7P
203999-56-8P, 3-[{2-(2-Nitrophenyl)furan-5-yl}methylidene}]-5-
(morpholinosulfonyl)-2-indolinone 203999-57-9P,
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3-[(9-Ethylcarbazol-3-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
203999-58-0P, 3-[(6,7-Dimethyl-1,4-benzopyron-3-yl)methylidenyl]-5-
(2-chloroethyl)-2-indolinone 203999-59-1P, 3-[[4-(Propen-2-
yl)cyclohexen-1-yl]methylidenyl]-5-(2-chloroethyl)-2-indolinone
203999-61-5P, 3-[(6-Isopropyl-1,4-benzopyron-3-yl)methylidenyl]-5-
(2-chloroethyl)-2-indolinone 203999-63-7P, 3-[(6-Methyl-1,4-
benzopyron-3-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
203999-65-9P, 3-[(6-Nitro-1,4-benzopyron-3-y1)methylidenyl]-5-(2-
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3-[(5-Methoxyindol-3-yl)methylidenyl]-5-(2-chloroethyl)-2-indolinone
203999-71-7P 203999-73-9P, 3-[[2-(2-Nitrophenyl)furan-5-
yl]methylidene]-5-(2-chloroethyl)-2-indolinone 203999-77-3P,
3-(3,5-Diisopropyl-4-methoxybenzylidenyl)-5,7-dibromo-2-indolinone
203999-79-5P, 3-(3,5-Diisopropyl-4-phenoxybenzylidenyl)-5,7-
dibromo-2-indolinone 203999-81-9P, 3-(3-tert-Butyl-4-
methoxybenzylidenyl)-5,7-dibromo-2-indolinone 203999-83-1P,
3-[4-(Benzyloxý)-3-tert-butylbenzylidenyl]-5,7-dibromo-2-indolinone
203999-85-3P, 3-(3-Bromo-5-tert-butyl-4-methoxybenzylidenyl)-5,7-
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tert-butylbenzylidenyl]-5,7-dibromo-2-indolinone 203999-89-7P,
3-(3-tert-Butyl-5-chloro-4-methoxybenzylidenyl)-5,7-dibromo-2-indolinone
203999-91-1P, 3-[4-(Benzyloxy)-5-tert-butyl-3-chlorobenzylidenyl]-
5,7-dibromo-2-indolinone 203999-93-3P, 3-(3-tert-Butyl-5-iodo-4-
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3-(3,5-Diisopropyl-4-methoxybenzylidenyl)-5-iodo-2-indolinone
203999-99-9P, 3-(3,5-Diisopropyl-4-phenoxybenzylidenyl)-5-iodo-2-
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5-iodo-2-indolinone 204000-03-3P, 3-[4-(Benzyloxy)-3-tert-
butylbenzylidenyl]-5-iodo-2-indolinone 204000-05-5P,
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204000-07-7P, 3-[4-(Benzyloxy)-3-bromo-5-tert-butylbenzylidenyl]-5-
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3-[4-(Benzyloxy)-5-tert-butyl-3-chlorobenzylidenyl]-5-iodo-2-indolinone
204000-17-9P, 3-(3-tert-Butyl-5-iodo-4-methoxybenzylidenyl)-5-iodo-
2-indolinone 204000-21-5P, 3-(3,5-Diisopropyl-4-
methoxybenzylidenyl)-5-bromo-4-methyl-2-indolinone 204000-23-7P,
3-(3,5-Diisopropyl-4-phenoxybenzylidenyl)-5-bromo-4-methyl-2-indolinone
204000-25-9P, 3-(3-tert-Butyl-4-methoxybenzylidenyl)-5-bromo-4-
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butylbenzylidenyl]-5-bromo-4-methyl-2-indolinone 204000-29-3P,
3-(3-Bromo-5-tert-butyl-4-methoxybenzylidenyl)-5-bromo-4-methyl-2-
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3-(3-tert-Butyl-5-chloro-4-methoxybenzylidenyl)-5-bromo-4-methyl-2-
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chlorobenzylidenyl]-5-bromo-4-methyl-2-indolinone 204000-36-2P,
3-(3-tert-Butyl-5-iodo-4-methoxybenzylidenyl)-5-bromo-4-methyl-2-
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methoxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
204000-39-5P, 3-(3,5-Diisopropyl-4-phenoxybenzylidenyl)-5-
[(methylamino)sulfonyl]-2-indolinone 204000-40-8P,
3-(3-tert-Butyl-4-methoxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-
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butylbenzylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
204000-42-0P, 3-(3-Bromo-5-tert-butyl-4-methoxybenzylidenyl)-5-
[(methylamino)sulfonyl]-2-indolinone 204000-43-1P,
3-[4-(Benzyloxy)-3-bromo-5-tert-butylbenzylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 204000-44-2P,
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3-(3-tert-Butyl-5-chloro-4-methoxybenzylidenyl)-5-[(methylamino)sulfonyl]-
2-indolinone 204000-45-3P, 3-[4-(Benzyloxy)-5-tert-butyl-3-
chlorobenzylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
204000-46-4P, 3-(3-tert-Butyl-5-iodo-4-methoxybenzylidenyl)-5-
[(methylamino)sulfonyl]-2-indolinone 204000-48-6P,
3-(3,5-Diisopropyl-4-methoxybenzylidenyl)-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 204000-49-7P
  3-(3,5-Diisopropyl-4-phenoxybenzylidenyl)-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 204000-50-0P
 3-(3-tert-Butyl-4-methoxybenzylidenyl)-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 204000-51-1P
 3-[4-(Benzyloxy)-3-tert-butylbenzylidenyl]-5-[[[4-
(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 204000-52-2P
  3-(3-Bromo-5-tert-butyl-4-methoxybenzylidenyl)-5-[[[4-
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  3-(3-tert-Butyl-5-iodo-4-methoxybenzylidenyl)-5-[[[4-
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204000-60-2P, 3-(3-tert-Butyl-4-methoxybenzylidenyl)-5-
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3-[4-(Benzyloxy)-3-tert-butylbenzylidenyl]-5-(morpholinosulfonyl)-2-
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204000-63-5P, 3-[4-(Benzyloxy)-3-bromo-5-tert-butylbenzylidenyl]-5-
(morpholinosulfonyl)-2-indolinone 204000-64-6P,
3-(3-tert-Butyl-5-chloro-4-methoxybenzylidenyl)-5-(morpholinosulfonyl)-2-
indolinone 204000-65-7P, 3-[4-(Benzyloxy)-5-tert-butyl-3-
chlorobenzylidenyl]-5-(morpholinosulfonyl)-2-indolinone
204000-66-8P, 3-(3-tert-Butyl-5-iodo-4-methoxybenzylidenyl)-5-
(morpholinosulfonyl)-2-indolinone 204000-68-0P,
3-(3,5-Diisopropyl-4-methoxybenzylidenyl)-5-(2-chloroethyl)-2-indolinone
204000-69-1P, 3-(3,5-Diisopropyl-4-phenoxybenzylidenyl)-5-(2-
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  3-[4-(Benzyloxy)-3-tert-butylbenzylidenyl]-5-(2-chloroethyl)-2-
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  3-[4-(Benzyloxy)-3-bromo-5-tert-butylbenzylidenyl]-5-(2-chloroethyl)-2-
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  3-[4-(Benzyloxy)-5-tert-butyl-3-chlorobenzylidenyl]-5-(2-chloroethyl)-2-
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  3-[4-(Benzyloxy)-3-tert-butyl-5-iodobenzylidenyl]-5,7-dibromo-2-
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3-(3,5-Di-tert-butyl-4-methoxybenzylidenyl)-5,7-dibromo-2-indolinone
204000-80-6P, 3-[4-(Benzyloxy)-3,5-di-tert-butylbenzylidenyl]-5,7-
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methoxybenzylidenyl)-5,7-dibromo-2-indolinone 204000-82-8P,
3-[4-(Benzyloxy)-3,5-dimethylbenzylidenyl]-5,7-dibromo-2-indolinone
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204000-83-9P, 3-(5-Bromo-2-hydroxy-3-methoxybenzylidenyl)-5,7-
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hydroxybenzylidenyl)-5,7-dibromo-2-indolinone 204000-85-1P,
3-(2-Hydroxy-5-nitrobenzylidenyl)-5,7-dibromo-2-indolinone
204000-86-2P, 3-(4-Hydroxy-3-methoxy-2-nitrobenzylidenyl)-5,7-
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5-iodobenzylidenyl]-5-iodo-2-indolinone 204000-88-4P,
3-(3-tert-Butyl-4-methoxy-5-nitrobenzylidenyl)-5-iodo-2-indolinone
204000-89-5P, 3-(3,5-Di-tert-butyl-4-methoxybenzylidenyl)-5-iodo-2-
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204000-92-0P, 3-[4-(Benzyloxy)-3,5-dimethylbenzylidenyl]-5-iodo-2-
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3-(5-Bromo-2-hydroxybenzylidenyl)-5-iodo-2-indolinone 204000-95-3P
   3-(2-Hydroxy-5-nitrobenzylidenyl)-5-iodo-2-indolinone
204000-96-4P, 3-(4-Hydroxy-3-methoxy-2-nitrobenzylidenyl)-5-iodo-2-
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3-[4-(Benzyloxy)-3,5-di-tert-butylbenzylidenyl]-5-bromo-4-methyl-2-
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3-(4-Hydroxy-3-methoxy-2-nitrobenzylidenyl)-5-bromo-4-methyl-2-indolinone
204001-07-0P, 3-[4-(Benzyloxy)-3-tert-butyl-5-iodobenzylidenyl]-5-
[(methylamino) sulfonyl]-2-indolinone 204001-08-1P,
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204001-10-5P, 3-[4-(Benzyloxy)-3,5-di-tert-butylbenzylidenyl]-5-
[(methylamino)sulfonyl]-2-indolinone 204001-11-6P,
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dimethylbenzylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone
204001-13-8P, 3-(5-Bromo-2-hydroxy-3-methoxybenzylidenyl)-5-
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3-(5-Bromo-2-hydroxybenzylidenyl)-5-[(methylamino)sulfonyl]-2-indolinone
204001-15-0P, 3-(2-Hydroxy-5-nitrobenzylidenyl)-5-
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3-(4-Hydroxy-3-methoxy-2-nitrobenzylidenyl)-5-[(methylamino)sulfonyl]-2-
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indolinone 204001-19-4P, 3-(3,5-Di-tert-butyl-4-
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indolinone 204001-21-8P, 3-[4-(Benzyloxy)-3,5-di-tert-
butylbenzylidenyl]-5-[[{4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
indolinone 204001-22-9P, 3-(3,5-Dimethyl-4-methoxybenzylidenyl)-
5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone
204001-23-0P, 3-[4-(Benzyloxy)-3,5-dimethylbenzylidenyl]-5-[[[4-
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(trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 204001-24-1P
        , 3-(5-Bromo-2-hydroxy-3-methoxybenzylidenyl)-5-[[[4-
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        , 3-(5-Bromo-2-hydroxybenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]s
       ulfonyl]-2-indolinone 204001-26-3P, 3-(2-Hydroxy-5-
       nitrobenzylidenyl)-5-[[[4-(trifluoromethyl)phenyl]amino]sulfonyl]-2-
        indolinone 204001-27-4P
, 3-(4-Hydroxy-3-methoxy-2-nitrobenzylidenyl)-5-[[[4-
        (trifluoromethyl)phenyl]amino]sulfonyl]-2-indolinone 204001-28-5P
           3-[4-(Benzyloxy)-3-tert-butyl-5-iodobenzylidenyl]-5-(morpholinosulfonyl)-
        2-indolinone 204001-29-6P, 3-(3-tert-Butyl-4-methoxy-5-.
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        (morpholinosulfonyl)-2-indolinone 204001-36-5P,
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       204001-37-6P, 3-(4-Hydroxy-3-methoxy-2-nitrobenzylidenyl)-5-
        (morpholinosulfonyl)-2-indolinone 204001-38-7P,
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       indolinone 204001-39-8P, 3-(3-tert-Butyl-4-methoxy-5-
       nitrobenzylidenyl)-5-(2-chloroethyl)-2-indolinone 204001-40-1P,
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       RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
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             (prepn. and testing of indolinone combinatorial library as protein
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        3-(3,5-Dibromo-2-hydroxybenzylidenyl)-5,7-dibromo-2-indolinone
        204001-54-7P, 3-(3-Fluoro-2-hydroxybenzylidenyl)-5,7-dibromo-2-
        indolinone 204001-55-8P, 3-(3-Bromo-4-hydroxybenzylidenyl)-5,7-
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Hunt 09 186475

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     204006-05-3P 204006-06-4P 204006-19-9P
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     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (prepn. and testing of indolinone combinatorial library as protein
        kinase inhibitors)
L18 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2001 ACS
                         1998:1471 HCAPLUS
ACCESSION NUMBER:
DOCUMENT NUMBER:
                         128:61437
                         Preparation of substituted quinolylmethylenoxoindole
TITLE:
                         analogs as tyrosine kinase inhibitors
                         Battistini, Carlo; Ermoli, Antonella; Vioglio, Sergio;
INVENTOR(S):
                         Buzzetti, Franco; Ballinari, Dario
                         Pharmacia + Upjohn S.p.A., Italy; Battistini, Carlo;
PATENT ASSIGNEE(S):
                         Ermoli, Antonella; Vioglio, Sergio; Buzzetti, Franco;
                         Ballinari, Dario
                         PCT Int. Appl., 51 pp.
SOURCE:
                         CODEN: PIXXD2
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Patent

DOCUMENT TYPE:

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO. KIND DATE APPLICATION NO. DATE WO 9746551 19971211 WO 1997-EP2673 19970515 A1 W: JP, US RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE EP 876365 Α1 19981111 EP 1997-927035 19970515 R: DE, GB, JP 11510823 T2 19990921 JP 1997-500166 19970515 US 5905149 19990518 US 1998-983516 19980129 Α PRIORITY APPLN. INFO.: GB 1996-11797 19960606 WO 1997-EP2673 19970515

OTHER SOURCE(S):

MARPAT 128:61437

·GI

The title compds. [I; R1-R4 = X(CH2)mNH2, X(CH2)mNR5R6, etc.; R = H, (CH2)nCOR7, etc.; n = 1-4; m = 2-4; R5, R6 = H, C1-6 alkyl; R7 = (un)substituted aminoacids, etc.] and the pharmaceutically acceptable salts thereof are prepd. I, possessing tyrosine kinase inhibitory activity, are useful as immunomodulating agents, and antimetastatic and anticancer agents, or in the control of angiogenesis and atheromatous plaque, and treatment of Alzheimer's disease. Thus, 8-hydroxyquinoline-5-carbaldehyde was reacted with 2-oxoindole in the presence of piperidine and then reacted with MeCHBrCO20Et in the presence of Bu4NF to give the title compd. (II), which showed IC50 of 39.5 .mu.M against K562 cell growth in vivo. A formulation contg. I were also prepd.

IT 200285-07-0P 200285-08-1P 200285-09-2P 200285-10-5P 200285-11-6P 200285-12-7P 200285-13-8P 200285-14-9P 200285-15-0P

200285-20-7P 200285-21-8P 200285-22-9P RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

(Preparation); USES (Uses)

(prepn. of substituted quinolylmethylenoxoindole analogs as tyrosine kinase inhibitors)

IT 137479-19-7P 168464-10-6P 200285-25-2P

200285-26-3P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. of substituted quinolylmethylenoxoindole analogs as tyrosine kinase inhibitors)

L18 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER:

1997:805721 HCAPLUS

DOCUMENT NUMBER:

128:61424

TITLE:

Preparation of substituted tetralinylmethylen-2oxoindole analogs as tyrosine kinase inhibitors

INVENTOR(S):

Battistini, Carlo; Ermoli, Antonella; Vioglio, Sergio;

Buzzetti, Franco; Ballinari, Dario

PATENT ASSIGNEE(S):

Pharmacia & Upjohn, S.p.A., Italy; Battistini, Carlo; Ermoli, Antonella; Vioglio, Sergio; Buzzetti, Franco;

Ballinari, Dario

SOURCE:

PCT Int. Appl., 43 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO. DATE	
WO 9745409	A1	19971204	WO 1997-EP2672 19970515	
W: JP, US				
RW: AT, BE,	CH, DE	, DK, ES,	FI, FR, GB, GR, IE, IT, LU, MC, NL, PT	, SE
EP 853614	A1	19980722	EP 1997-927034 19970515	
EP 853614	В1	20011004		
R: DE, GB,	ΙT			
JP 11510822	Т2	19990921	JP 1997-541580 19970515	
US 6147073	Α	20001114	US 1998-981473 19980112	
PRIORITY APPLN. INFO	.:		GB 1996-10964 A 19960524	
			WO 1997-EP2672 W 19970515	

OTHER SOURCE(S):

MARPAT 128:61424

GI

$$R^2$$
 R^2
 R^3
 R^3

AB The title compds. [I; R, R1-R3 = X(CH2)mNH2, X(CH2)mNR4R5, etc.; X = O, S, NH, etc.; m = 2-4; R4, R5 = H, C1-6 alkyl, etc.] and pharmaceutically acceptable salts thereof are prepd. I, possessing tyrosine kinase inhibitory activity, are useful as antiproliferative, anti-metastatic, immunomodulating, and anticancer agents, or in the control of angiogenesis and in the treatment of Alzheimer's diseases. Thus,

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I (R = R1 = R3 = H, R2 = 5-NH2) (prepn. given) was reacted with N-tert-butoxycarbonyl-L-qlutamic acid tert-Bu ester in the presence of benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate and N-methylmorpholine, and then treated with CF3CO2H to give 40% I.CF3CO2H (R, R1, R3 = same as above, R2 = glutamylamino), which showed IC50 of 5.97.mu.M against K562 cell growth in vivo. A formulation contg. I were IT 200191-17-9P 200191-19-1P 200191-21-5P 200191-23-7P 200191-25-9P 200191-27-1P 200191-29-3P RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of substituted tetralinylmethylen-2-oxoindole analogs as tyrosine kinase inhibitors) ΙT 200191-30-6P 200191-34-0P RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation) (prepn. of substituted tetralinylmethylen-2-oxoindole analogs as tyrosine kinase inhibitors) L18 ANSWER 16 OF 17 HCAPLUS COPYRIGHT 2001 ACS 1996:746204 HCAPLUS ACCESSION NUMBER: DOCUMENT NUMBER: 126:18783 Substituted indolylmethylene-oxindole analogs as TITLE: tyrosine kinase inhibitors Battistini, Carlo; Ballinari, Dario; Ermoli, INVENTOR(S): Antonella; Penco, Sergio; Vioglio, Sergio PATENT ASSIGNEE(S): Pharmacia S.P.A., Italy PCT Int. Appl., 53 pp. SOURCE: CODEN: PIXXD2 DOCUMENT TYPE: Patent English LANGUAGE: FAMILY ACC. NUM. COUNT: PATENT INFORMATION: PATENT NO. KIND DATE APPLICATION NO. DATE 19961017 WO 1996-EP1165 WO 9632380 Α1 19960314 W: JP, US RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE A1 19970326 EP 1996-907500 19960314 R: DE, ES, FR, GB, IT, SE JP 10501821 T2 19980217 JP 1996-530667 19960314 US 5849710 Α 19981215 US 1996-750208 19961204 PRIORITY APPLN. INFO.: GB 1995-7298 19950407

WO 1996-EP1165

19960314

MARPAT 126:18783

OTHER SOURCE(S):

GI

AB Indol-3-ylmethylene-2-oxindole derivs. I and their pharmaceutically acceptable salts are disclosed [wherein 1 or 2 of R, R1, R2, and R3 = X(CH2)mNH2, X(CH2)mNR4R5, X(CH2)mNHR6, NHC(:NH)NH2, NHC(:NH)NR4R5, NHC(:NH)NHR6, N:CHNH2, N:CHNR4R5, N:CHNHR6, X(CH2)mCOR7, CORa, COR8, YCOY'R9, NHR6, NHR10 group; remaining groups within R and R1-R3 = H, halo, amino, OH, alkyl, alkoxy, CO2H, alkoxycarbonyl, alkanoyloxy, cyano, NR4R5; X = O, S, NH; m = 1-4; 1 of R4 and R5 = H or alkyl, and other = alkyl; or NR4R5 forms satd. monoheterocycle; R6 = alkanoyl, 1- to 3-residue (un) substituted peptidyl; R7 = OH, amino, alkoxy, NR4R5; Ra = amino terminus of 1- to 3-unit peptidyl; R8 = alkoxy, phenylalkoxy, (CH2)nNH2, (CH2) nNR4R5, (CH2) nNHR6; n = 1-2; Y, Y' = NH, O; R9 = Ph, alkyl, phenylalkyl; R10 = mono-, di- or trihydroxyalkyl]. I have tyrosine kinase inhibiting activity, and are useful as antiproliferative, antimetastatic, anticancer, antiatheromatous, anti-Alzheimer, and immunomodulating agents. For example, 2-indolinone reacted with BrCH2COBr and AlCl3 to give the 5-(2-bromoacetyl) deriv., which underwent amination with piperidine and then condensation with indole-3-carboxaldehyde, to give title compd. II (FCE 28484). In tests for inhibition of p45 v-abl kinase and K562 leukemia cells in vitro, II had IC50 of 0.78 and 4.82 .mu.M, resp.

IT 168464-17-3P 184021-39-4P 184021-56-5P 184021-79-2P 184021-85-0P 184021-97-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
 (intermediate; prepn. of (indolylmethylene)oxindole analogs as tyrosine
 kinase inhibitors)

IT 184020-98-2P

RL: BAC (Biological activity or effector, except adverse); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of (indolylmethylene)oxindole analogs as tyrosine kinase inhibitors)

IT 181223-99-4P 184020-79-9P 184020-86-8P

184020-93-7P 184021-06-5P 184021-15-6P

184021-23-6F

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of (indolylmethylene)oxindole analogs as tyrosine kinase inhibitors)

IT 184020-69-7P

RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP

Hunt 09 186475

(Preparation); USES (Uses)

(prepn. of (indolylmethylene)oxindoles as tyrosine kinase inhibitors)

L18 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2001 ACS

ACCESSION NUMBER: DOCUMENT NUMBER:

1995:828284 HCAPLUS 123:227985

TITLE:

Arylidene and heteroarylidene oxindole derivatives as

tyrosine kinase inhibitors

INVENTOR(S):

Buzzetti, Franco; Longo, Antonio; Brasca, Maria

Gabriella; Orzi, Fabrizio; Crugnola, Angelo; Ballinari, Dario; Mariani, Mariangela

Farmitalia Carlo Erba S.r.l., Italy

PATENT ASSIGNEE(S):

PCT Int. Appl., 62 pp.

SOURCE:

DOCUMENT TYPE:

CODEN: PIXXD2

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	ENT NO.		KIND		APPLICATION NO. DATE	
WO	9501349				WO 1994-EP1715 19940526	
					CN, CZ, FI, HU, JP, KP, KR, KZ, LK, LV	7,
					RO, RU, SD, SK, UA, UZ, VN	
					FR, GB, GR, IE, IT, LU, MC, NL, PT, SE	3
CA	2142472		AA	19950112	CA 1994-2142472 19940526	
AU	9469719		A1	19950124	AU 1994-69719 19940526	
AU	679754		B2	19970710		
					EP 1994-918379 19940526	
EP	658159		B1	20000823	•	
					FR, GB, GR, IE, IT, LI, NL, PT, SE	
CN	1111454		A	19951108	CN 1994-190452 19940526	
JP	08500847	,	Т2	19960130	JP 1994-503150 19940526	
HU	72047		. A2	19960328	HU 1995-954 19940526	
EP	987263		A2	20000322	EP 1999-203366 19940526	
	R: AT,	ΒE,	CH, DE	, DK, ĖS,	FR, GB, GR, IT, LI, NL, SE, PT, IE	
AT	195734		E	20000915	AT 1994-918379 19940526	
ES	2152317		тЗ	20010201	ES 1994-918379 19940526	
US	5656654		Α	19970812	ES 1994-918379 19940526 US 1994-263666 19940622	
ZA	9404730		A	19950713	ZA 1994-4730 1994.0630	
FI	9500859		Α	19950224	FI 1995-859 19950224	
RIORITY	APPLN.	INFO	.:		GB 1993-13638 A 19930701	
					EP 1994-918379 A3 19940526	
					WO 1994-EP1715 W 19940526	

OTHER SOURCE(S):

MARPAT 123:227985

Ι

$$(R^{10})_{n}$$
 $R^{3}-Y-CH$
 R^{4}

Title derivs. I [Y = naphthalene, tetralin, quinoline or isoquinoline system; R = H, plus oxo when Y is tetralin; R1, R2 independently = H, C1-6 alkyl or C2-6 alkanoyl; m = 0-2; n = 0-3; R3 independently = H, halo, cyano, C1-6 alkyl, carboxy, nitro or NR6R7 where R6, R7 independently = H, C1-6 alkyl; R5 = H, C1-6 alkyl] and their pharmaceutically acceptable salts, which are useful as tyrosine kinase inhibitors, are claimed. The E- and Z-isomers of approx. 85 compds. are specifically claimed. Several synthetic examples are given. For example, condensation of 8-hydroxyquinoline-5-carboxaldehyde with 5-hydroxy-2-oxindole in EtOH in the presence of piperidine at 60-70.degree. gave 60% title compd. II (R8 = OH). Among test results for 10 selected I for inhibition of p45 v-abl kinase in vitro, and for inhibition of cultured K562 human leukemia cell growth, II (R8 = Br) had IC50 values of 2.6 and 0.62 .mu.M, resp.

149492-63-7P 168462-84-8P 168462-85-9P 168462-86-0P 168462-87-1P 168462-88-2P 168462-89-3P 168462-90-6P 168462-91-7P 168462-92-8P 168462-93-9P 168462-94-0P 168462-95-1P 168462-96-2P 168462-97-3P 168462-98-4P 168462-99-5P 168463-00-1P 168463-01-2P 168463-02-3P 168463-03-4P 168463-04-5P 168463-05-6P 168463-06-7P 168463-07-8P 168463-08-9P 168463-09-0P 168463-10-3P 168463-11-4P 168463-12-5P 168463-13-6P 168463-14-7P, FCE 28360 168463-15-8P 168463-16-9P 168463-17-0P 168463-18-1P 168463-19-2P 168463-20-5P 168463-21-6P 168463-22-7P 168463-23-8P 168463-24-9P 168463-25-0P 168463-26-1P 168463-27-2P 168463-28-3P 168463-29-4P 168463-30-7P 168463-31-8P 168463-32-9P 168463-33-0P 168463-34-1P 168463-35-2P 168463-36-3P 168463-37-4P 168463-38-5P 168463-39-6P 168463-40-9P 168463-41-0P 168463-42-1P 168463-43-2P 168463-44-3P 168463-45-4P 168463-46-5P 168463-47-6P

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     168464-03-7P 168464-10-6P, FCE 27518
     168464-11-7P, FCE 27566 168464-12-8P, FCE 27565
     168464-13-9P, FCE 27866 168464-14-0P, FCE 27564
     168464-15-1P, FCE 27996 168464-16-2P, FCE 28359
     168464-17-3P, FCE 28436 168464-18-4P
     168464-19-5P 168464-20-8P 168464-21-9P
     168464-22-0P 168464-23-1P
     RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic
     preparation); THU (Therapeutic use); BIOL (Biological study); PREP
     (Preparation); USES (Uses)
        (invention compd.; prepn. of (hetero)arylidene oxindole derivs. as
        tyrosine kinase inhibitors)
     168464-07-1 168464-08-2 168464-09-3
TΥ
     RL: RCT (Reactant)
        (starting material; prepn. of (hetero)arylidene oxindole derivs. as
        tyrosine kinase inhibitors)
=> select hit rn 118 1-17
E# OR SYSTEM LIMIT REACHED WHILE PROCESSING ANSWER 13
E82 THROUGH E999 ASSIGNED
=> fil reg
FILE 'REGISTRY' ENTERED AT 09:14:58 ON 16 OCT 2001
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2001 American Chemical Society (ACS)
STRUCTURE FILE UPDATES:
                          14 OCT 2001 HIGHEST RN 362009-74-3
DICTIONARY FILE UPDATES: 14 OCT 2001
                                      HIGHEST RN 362009-74-3
TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001
  Please note that search-term pricing does apply when
  conducting SmartSELECT searches.
Crossover limits have been increased. See HELP CROSSOVER see
HELP CROSSOVER for details.
Calculated physical property data is now available. See HELP PROPERTIES
for more information. See STNote 27, Searching Properties in the CAS
Registry File, for complete details:
http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf
=> select hit rn 118 13-17
```

E# OR SYSTEM LIMIT REACHED WHILE PROCESSING ANSWER 13 E1 THROUGH E999 ASSIGNED

=> del select y

=> select hit rn 118 13

E# OR SYSTEM LIMIT REACHED WHILE PROCESSING ANSWER 13

E1 THROUGH E999 ASSIGNED

=> delete select y
ALL E# DEFINITIONS DELETED

=> select hitrn 118 14-17
'HITRN' IS NOT A VALID FIELD CODE FOR FILE 'HCAPLUS'
ENTER DISPLAY CODE (TI) OR ?:end

=> select hit rn l18 14-17 E1 THROUGH E163 ASSIGNED

=> fil reg FILE 'REGISTRY' ENTERED AT 09:21:38 ON 16 OCT 2001 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2001 American Chemical Society (ACS)

STRUCTURE FILE UPDATES: 14 OCT 2001 HIGHEST RN 362009-74-3 DICTIONARY FILE UPDATES: 14 OCT 2001 HIGHEST RN 362009-74-3

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER see HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details: http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf

=> =>

=> d his 119-121

(FILE 'HCAPLUS' ENTERED AT 09:08:11 ON 16 OCT 2001) SELECT HIT RN L18 1-17

FILE 'REGISTRY' ENTERED AT 09:14:58 ON 16 OCT 2001 L19 918 S E82-E250 OR E251-E500 OR E501-E750 OR E751-999

FILE 'HCAPLUS' ENTERED AT 09:19:55 ON 16 OCT 2001

DEL SELECT

SELECT HIT RN L18 13-17

DEL SELECT Y

SELECT HIT RN L18 13

DELETE SELECT Y

SELECT HIT RN L18 14-17

FILE 'REGISTRY' ENTERED AT 09:21:38 ON 16 OCT 2001

L20 1080 S E1-E163 OR L19

L21 1079 S L5 AND L20

=> =>

=> d ide can 121 1 100 200 300 400 500 600 700 800 900 1000 1079

L21 ANSWER 1 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN 358733-27-4 REGISTRY

CN 1H-Indole-5-sulfonamide, 2,3-dihydro-N,N-dimethyl-2-oxo-3-[(4,5,6,7-tetrahydro-5-methyl-4-oxo-2H-pyrrolo[3,4-c]pyridin-1-yl)methylene]- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C19 H20 N4 O4 S

SR CA

LC STN Files: CA, CAPLUS

$$\begin{array}{c|c}
 & H & O & HN & Me \\
Me_2N-S & & & & \\
Me_2N-S & & & & \\
0 & & & & & \\
\end{array}$$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:226880

L21 ANSWER 100 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN 356069-30-2 REGISTRY

CN 1H-Pyrrole-3-carboxamide, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2,4-dimethyl-N-[3-(tetrahydro-2-oxo-1(2H)-pyrimidinyl)propyl]- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C23 H27 N5 O3

SR CA

LC STN Files: CA, CAPLUS

Double bond geometry as shown.

$$\begin{array}{c|c} & & & \\ &$$

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:195497

L21 ANSWER 200 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN **342641-53-6** REGISTRY

CN 1H-Pyrrole-3-carboxylic acid, 5-[(5-bromo-1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-2-(1-methylethyl)-4-phenyl- (9CI) (CA INDEX NAME)

FS 3D CONCORD

MF C23 H19 Br N2 O3

SR CA

LC STN Files: CA, CAPLUS

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

2 REFERENCES IN FILE CA (1967 TO DATE)

2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:195497

REFERENCE 2: 135:19549

L21 ANSWER 300 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN 280748-39-2 REGISTRY

CN 1H-Pyrrole-2-carboxylic acid, 5-[(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN SU 6595

FS 3D CONCORD

MF C15 H12 N2 O3

SR CA

LC STN Files: CA, CAPLUS, TOXLIT

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

5 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA

5 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 135:195497

REFERENCE 2: 135:107247

REFERENCE 3: 135:19549

REFERENCE 4: 134:141334

REFERENCE 5: 133:84238

L21 ANSWER 400 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN 210303-50-7 REGISTRY

CN 1H-Pyrrole-3-propanoic acid, 5-[(Z)-(1,2-dihydro-2-oxo-3H-indol-3-ylidene)methyl]-4-methyl- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C17 H16 N2 O3

SR CA

LC STN Files: CA, CAPLUS, TOXLIT

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE) 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 129:117426

L21 ANSWER 500 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN 203992-55-6 REGISTRY

CN 2H-Indol-2-one, 5-bromo-1,3-dihydro-4-methyl-3-[[4-(trifluoromethyl)phenyl]methylene]- (9CI) (CA INDEX NAME) OTHER NAMES:

CN 3-[4-(Trifluoromethyl)benzylidene]-5-bromo-4-methyl-2-indolinone

MF C17 H11 Br F3 N O

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:204803

L21 ANSWER 600 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN 203991-55-3 REGISTRY

CN 2H-Indol-2-one, 5-(2-chloroethyl)-1,3-dihydro-3-(1H-imidazol-2-ylmethylene)- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 3-[(Imidazol-2-yl)methylene]-5-(2-chloroethyl)-2-indolinone

FS 3D CONCORD

MF C14 H12 C1 N3 O

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:204803

L21 ANSWER 700 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN 203990-24-3 REGISTRY

CN 1H-Indole-5-sulfonamide, 3-[[4-fluoro-2-(trifluoromethyl)phenyl]methylene]-2,3-dihydro-N-methyl-2-oxo-(9CI) (CA INDEX NAME)

OTHER NAMES:

CN 3-[4-Fluoro-2-(trifluoromethyl)benzylidenyl]-5-[(methylamino)sulfonyl]-2-indolinone

FS 3D CONCORD

MF C17 H12 F4 N2 O3 S

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:204803

L21 ANSWER 800 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN 203989-13-3 REGISTRY

CN 2H-Indol-2-one, 5,7-dibromo-3-(2-furanylmethylene)-1,3-dihydro- (9CI) (CA INDEX NAME)

OTHER NAMES:

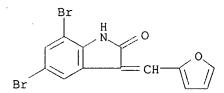
CN 3-(Furan-2-ylmethylidenyl)-5,7-dibromo-2-indolinone

FS 3D CONCORD

MF C13 H7 Br2 N O2

SR CA

LC STN Files: CA, CAPLUS, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967. TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:204803

L21 ANSWER 900 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN 200191-19-1 REGISTRY

CN 2H-Indol-2-one, 5-amino-1,3-dihydro-3-[(5,6,7,8-tetrahydro-1,4-dihydroxy-2-naphthalenyl)methylene]-, mono(trifluoroacetate) (salt) (9CI) (CA INDEX NAME)

MF C19 H18 N2 O3 . C2 H F3 O2

SR CA

LC STN Files: CA, CAPLUS, USPATFULL

CM 1

CRN 200191-18-0 CMF C19 H18 N2 O3

$$H_2N$$
 O
 OH
 OH
 OH

CM 2

CRN 76-05-1 CMF C2 H F3 O2

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 128:61424

L21 ANSWER 1000 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN 168463-44-3 REGISTRY

CN 2H-Indol-2-one, 1,3-dihydro-5-hydroxy-3-[(5-methoxy-1H-indol-3-yl)methylene]-, (E)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C18 H14 N2 O3

SR CF

LC STN Files: CA, CAPLUS, USPATFULL

Double bond geometry as shown.

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1967 TO DATE)

1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 123:227985

L21 ANSWER 1079 OF 1079 REGISTRY COPYRIGHT 2001 ACS

RN 5812-07-7 REGISTRY

CN 2H-Indol-2-one, 3-[[4-(dimethylamino)phenyl]methylene]-1,3-dihydro- (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 2-Indolinone, 3-[p-(dimethylamino)benzylidene]- (7CI, 8CI)

OTHER NAMES:

CN 3-(4-Dimethylaminobenzylidenyl)-2-indolinone

CN SU 4312

MF C17 H16 N2 O

LC STN Files: BEILSTEIN*, BIOSIS, CA, CAOLD, CAPLUS, CHEMCATS, TOXLIT, USPATFULL

(*File contains numerically searchable property data)

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

13 REFERENCES IN FILE CA (1967 TO DATE)

13 REFERENCES IN FILE CAPLUS (1967 TO DATE)

1 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 133:234344

REFERENCE 2: 130:348928

REFERENCE 3: 130:252240

REFERENCE 4: 130:237471

REFERENCE 5: 130:237470

REFERENCE 6: 130:149064

REFERENCE 7: 129:330650

REFERENCE 8: 129:175549

REFERENCE 9: 127:314804

REFERENCE 10: 126:139901